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## TREATMENT OF BREAST ABSCESSES WITH PENICILLIN


BY

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IN COLLABORATION WITH

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The following account deals with various methods of treating breast abscesses with penicillin. The justification of those methods depended on their results as compared with those obtained from the methods at present employed. For this reason a series of controls was treated contemporaneously with the penicillin series and the two were compared not only as to the average duration of pyrexia, suppuration, and healing time, summarized in the accompanying Table, but also with regard to a number of other points which were considered important. The apparent advantages obtained by the use of penicillin would seem to justify a detailed description of the methods of administration found most satisfactory.

*Table Comparing Results in Breast Abscesses*

| | No. of Cases | Duration in Days after First Treatment of: Pyrexia Mean ± S.E. | Pyrexia S.D. | Suppuration Mean ± S.E. | Suppuration S.D. | Healing Time Mean ± S.E. | Healing Time S.D. |
|---|---|---|---|---|---|---|---|
| Controls . | 16* | 7·5 ±1·97 | ±7·86 | 13·8±3·0 | ±12·0 | 26·5‡±2·45 | ±10·17 |
| Treated . | 18 | 3·9†±0·91 | ±3·73 | 6·3±0·82 | ± 3·5 | 13·5 ± 1·50 | ± 6·37 |
| Difference | | 3·6 ±2·17 | | 7·5±3·11 | | 13·0 ±2·87 | |

S.E. = Standard error of mean. S.D. = Standard deviation.
* Two control cases excluded, because in Case 1 the follow-up was not conclusive, and in Case 2 the duration of pyrexia was 63 days, suppuration >88 days, and healing >119 days.
† Mean of 17 cases only; no record of 18th case.
‡ Mean of healing time of abscesses in 17 breasts.

The survey comprised all cases which came under treatment at the Central Middlesex County Hospital between Nov. 19, 1943, and May 18, 1944. They were nursed in the obstetric or surgical wards according to whether their symptoms arose during the puerperium or later. Both series were cared for by the same nursing staff and the same surgeons. The cases numbered 36, and, in order to eliminate any bias on the part of the investigators, they were chosen for the control or penicillin series in strictly alternate chronological order. There were 22 abscesses in the 18 control cases and 24 in the 18 penicillin-treated cases. Factors which might have favoured one series more than the other were also noted. The time of onset in relation to parturition was within the first fortnight in 6 control and 7 penicillin-treated abscesses, and a further 9 and 7 respectively arose within five weeks of the same date. The incidence in primiparae was half the total in each series. The age incidence was somewhat lower and the onset more often rapid in the penicillin cases, and pyrexia from other causes during the puerperium was present in 4 of the latter. Extraneous factors therefore could not be said to have favoured the penicillin group.

No case was accepted for investigation unless a well-defined, tender, and indurated mass was palpable in the breast tissue. Several cases examined during the puerperium, with flushed and tender breasts, some pyrexia, but ill-defined induration, were excluded as not giving sufficient evidence of infection. These did in fact clear up without chemotherapy, by the usual methods of elevation of the breast and the application of ice-bags. The distinction, however, was not always easy to make, and one case in which induration was not well defined was included in the controls.

### Methods of Treatment

Controls, with two exceptions, received at least one course of sulphathiazole or sulphamezathine of between 20 and 30 g. This was begun pre-operatively when abscesses were not well localized, incision being carried out later at the surgeon's discretion. When fluctuation could be detected on admission, incisions were made immediately—single for small abscesses and with a counter-incision for larger ones. Drainage was maintained by a corrugated rubber drain or a vaselined-gauze wick for 48 hours. Subsequently the wounds were dressed or irrigated with eusol, and when they became superficial flavine and paraffin or lotio rubra were generally used. A course of stilboestrol varying from 30 to 65 mg. in 3 to 5 days was given to patients who were lactating.

The penicillin cases were treated according to the type of case and, as the investigation progressed, also to the lessons learnt from earlier mistakes. No sulphonamides were given, and stilboestrol was administered to only 3 cases, all in the early stages of the inquiry. The methods are described in detail below.

### Items of Comparison

1. *Bacteriological Findings.—Staph. aureus* was the only organism found at operation in the abscesses with no external communication. One which had arisen from the residual sinus of an earlier abscess was, however, infected with a haemolytic streptococcus alone. Milk from six infected breasts was examined and found to contain *Staph. aureus* in each instance. The pus from one case in the control series was sterile on culture at operation and revealed no organism but *Bact. coli* in subsequent cultures. It is as well to mention that a phenomenon noticed in other acute infections was also noted here on several occasions—namely, that some swabs taken from pus at the time of the first incision were sterile on culture and yet cultures made later from swabs of the wound walls produced an abundant growth of *Staph. aureus*. Subsequent swabbings were made at weekly intervals in the controls and as soon as pus had disappeared in the penicillin-treated cases—i.e., from the second to the thirteenth day after the first local treatment. In the controls *Staph. aureus* persisted in 18 of 21 abscesses followed up till healing was nearly complete, and disappeared in 18 out of 20 "treated" abscesses before treatment was discontinued. The time of disappearance was anything from the second to the fifteenth day of treatment.


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The disappearance of pus from the exudate coincided closely with the disappearance of *Staph. aureus* from cultures. In fact, it was soon realized that in these staphylococcal infections the taking of a swab for culture was simply a way of confirming the clinical finding that the replacement of pus by a sero-sanguineous exudate signified that the abscess walls were no longer infected.

Secondary infection with *Str. haemolyticus* occurred in 3 control cases, the healing times of two of these being prolonged much beyond the average. No penicillin-treated cases became so infected. The remaining secondary invaders—*Staph. albus, Micrococcus tetragenus, Bact. coli,* and *Proteus*—appeared in 7 control and 5 penicillin-treated series, the Gram-negatives occurring in the same number—2—of each series. No clinical significance could be attached to the presence of these organisms, as they appeared only when wounds were superficial and healing.

2. *Suppuration* seemed to have been prevented by sulphonamide administration in one control case for several weeks, but after discharge from hospital this patient reported again with a painful lump in her breast. Unfortunately she was lost sight of after this. In some instances it appeared that pus formation was prevented or at least reduced by the use of sulphonamides. No frank pus was found in 3 cases. A fourth had a virulent infection in several loculi of one breast which spread later to the other. She received intensive courses of sulphamezathine and sulphathiazole, and pus was found in quantity only at the first incision, subsequent incisions into large swellings revealing only small amounts of sero-pus. In spite of this, however, once pus had formed in an abscess it continued till healing was well advanced. No case treated with penicillin at the stage already defined avoided the formation of pus. In fact, suppuration seemed to be speeded up and, while it localized readily, the pus became much thicker than in any of the control cases. It disappeared quickly, however, so that its average duration was less than half that of the controls.

3. *Twenty-two operations* were performed on 17 of the 18 controls, 5 cases requiring later incisions owing to extension of the infection. In all, 32 incisions were made. There were 4 operations in the penicillin-treated series and 4 incisions.

4. *Pyrexia* at the beginning of treatment varied very much from case to case, being little more than 99° F. (37.2° C.) where abscesses were already well localized, but reaching 103° F. (39.4° C.) in those whose infection arose in the puerperium. There were 5 cases in each series whose initial temperature rose above 101° F. (38.3° C.), the remainder all having milder degrees of pyrexia. The average duration after penicillin treatment, however, was reduced to half that of the controls. This was not because the penicillin-treated cases necessarily reached normal ranges before the controls, but because, once normal, their temperature did not rise again, as happened in several of the latter.

5. *Complications* in controls consisted of secondary abscesses in the same or the opposite breast or in axillary glands in 6 instances, and septic dermatitis in 3, while the infection in one long-standing case spread to the lids and the patient suffered from a persistent blepharitis. In the "treated" series two secondary abscesses developed, both in cases receiving local treatment only. A milk sinus persisted in a third case, prolonging the healing time to that of the average for the controls.

6. *Healing time* was estimated from the beginning of treatment, chemotherapeutic or surgical, till no further dressing or other local treatment was needed. In the case of open wounds or sinuses the end-point was the day on which the wound became quite dry ; in abscesses that were aspirated it was the day after the last aspiration on which any fluid could be withdrawn, no further treatment then being required. Where several abscesses were present in one breast the healing time covered the period from first treatment till the last abscess was healed. But if abscesses were present in both breasts their healing times were assessed separately (see Table).

Two patients had to be excluded from the control series—one because, though the induration and pyrexia appeared to subside under sulphonamide therapy, she later reported to the out-patient department with a painful lump in her breast ; but thereafter she could not be traced. The second patient had so severe and prolonged a convalescence that her healing time would have upset any reasonable comparison of the two series. There were no exclusions in the penicillin-treated series. After their abscesses had healed all these cases were followed up for from one to six weeks, according to the severity of the initial lesion. The healing times were therefore considered genuine, and they showed that not only was their average reduced to one-half that of the controls but that only one of all the penicillin-treated cases exceeded the average time for the controls.

7. *Breast feeding* had to be stopped in the majority of controls who were lactating. In the penicillin-treated cases, once confidence in the method of treatment had been gained, the avoidance of stilboestrol gave the mothers every opportunity to continue feeding their babies on the normal breast throughout treatment and to resume with the other after it had healed. In one case suckling was difficult because of retraction of the nipple following a persistent milk sinus, but in others the lack of scarring and retraction was in marked contrast to that of some of the controls. Induration in penicillin-treated cases, especially around those abscesses which were only aspirated, persisted for up to five weeks after treatment was begun ; but it eventually resolved, and after this time it was difficult to detect any indication that an abscess had existed.

8. *Days in Hospital.*—A final assessment was made of the days spent in hospital by the two series and also of the period of time during which they had to attend the out-patient department for treatment. These were as follows:

| | Control | Treated |
|---|---|---|
| Total number of days spent in hospital .. .. | 348 | 191 |
| Total period of out-patient treatment .. .. | 313 | 41 |
| Total .. .. .. .. .. | 661 | 232 |

Only 4 penicillin-treated cases had any out-patient treatment, though undoubtedly a good part of the treatment all received as in-patients could have been carried out effectively by daily attendance at the hospital. The need for accurate and frequent observation when a new method of treatment was being used, however, impelled their retention until it was possible to claim with assurance that these methods, when systematically used, were not only devoid of serious consequences but gave reliable results.

### Methods of Treatment with Penicillin

These depended on the condition of the breast when the patient was first seen. The choice of dose—for systemic or local effect—depended on whether or not the infection was still in the acute spreading stage with attendant constitutional disturbance. The method of treatment depended on whether an abscess had formed and on the amount of pus present.

*Intramuscular Injections of 15,000 Units Three-hourly (13 Cases).*—These were used for the acute phase before fluctuation could be detected, also when there was much pyrexia and a generalized flush over the breast, and for all infections arising in the puerperium. (Two cases with puerperal abscesses, not so treated initially, demonstrated the necessity for systemic treatment in acutely spreading lesions.) Injections were continued for a minimum of 12 hours, but no case required them for more than 3½ days. An injection was given pre-operatively immediately before any incision or exploration was carried out. The intramuscular treatment was stopped as soon as the pain had diminished, the flush began to fade, the oedema to lessen, and the pyrexia to subside.

*Aspiration and Injection of Penicillin under Local Analgesia once in 24 hours (10 Abscesses).*—This method was employed as soon as any fluctuation could be detected, and was even attempted without definite signs in deep and small abscesses which appeared to have localized. No spread of inflammation occurred after these explorations, but the patient always had penicillin circulating in her blood stream from an intramuscular injection given immediately before they were carried out. The aspiration was done with a wide-bore needle—a West Middlesex transfusion type containing a stylet was found satisfactory, as the needle could not become blocked before it had penetrated the abscess cavity. The area of maximum redness and swelling was avoided and the needle inserted obliquely from

where the skin was firm. A syringe having been attached to the needle after withdrawal of the stylet, all possible pus was aspirated. A second syringe containing the penicillin solution then replaced that used for aspiration, and an amount was injected equal to two-thirds the volume of the pus aspirated. If no pus was found a small amount of penicillin was injected into the tissues and along the needle track as the needle was withdrawn.

These aspirations and injections did not overlap the intramuscular treatment in any case by more than 24 hours, the assumption being that once pus was localized there was no need for further intramuscular treatment. When any doubt about complete localization existed, and when it was possible to inject a full 24-hour dose without leakage, 120,000 units, made up at the bedside in the required quantity of saline, were injected into the abscess cavity. Such a dose ensured a circulating concentration of penicillin for at least 12 hours (Florey and Heatley, 1945). By this method of systemic treatment three abscesses in one breast received treatment by injections into one only, until all had localized and could be treated individually. Where the abscess was well localized a concentration of 500 units per ml. was quite sufficient to sterilize the infected tissues. If no sinus formed this process was repeated every 24 hours till the pus, which became thicker and more slimy during the first two or three days of treatment, disappeared and was replaced by slimy blood-stained and then sero-sanguineous fluid. On the appearance of a sero-sanguineous exudate a film and a culture were made from the fluid, and if *Staph. aureus* was not present in either no further treatment was carried out. The breast was palpated carefully each day for at least a week and signs of recrudescence were looked for in temperature, flush, tenderness, or increasing induration. There was no recurrence in any of the cases so treated, but it should be remembered that treatment was never considered completed without confirmation of a sterile culture. Abscesses so treated contained no more than 10 ml. of pus and required daily injections for 4 to 7 days, irrespective of whether or not preliminary intramuscular treatment was necessary.

*Instillations of Penicillin after Expression of Pus (5 Abscesses).*—These instillations were most frequently made through a sinus which formed where the abscess pointed. This occurred very rapidly under the influence of penicillin therapy, and on the 24-hourly-aspiration-and-injection schedule it was often impossible to prevent sinuses developing. They were, however, of considerable value in treating the case, because the abscess cavity could now be emptied twice a day by gentle pressure and instillation carried out as often. In the interval, the mouth of the sinus was covered with cotton-wool soaked in collodion to prevent the egress of solution. Instillations were made by means of a fine rubber tube, nasal or ureteric catheter size, or by means of a West Middlesex needle, the important point being that the tube should completely occlude the mouth of the sinus to prevent escape of the solution during the injection.

*A combination of the two methods of local treatment* was used in 5 abscesses, instillations being made once a sinus had developed along the track of the aspirating needle. After aspiration a West Middlesex needle was left in the abscess cavity and fixed in place under a sterile dressing so that a second evacuation and instillation could be performed by the nursing staff in the absence of the medical attendant (Fig. 1). A sinus developed along this track in a day or two. At each subsequent treatment discharge was first expressed through the sinus, and the needle could then be inserted without local analgesia and by unskilled hands. The disadvantage of sinus formation over aspiration alone was the fact that it added a week to the healing time, but this was offset by the greater comfort of the treatment and the fact that it could be repeated more often, thus getting rid of purulent exudate quickly and so hastening the subsidence of infection.

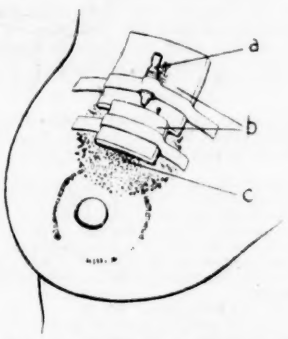


FIG. 1.—Treatment by indwelling cannula. Small breast abscess tending to point at *c*. *a*: West Middlesex needle inserted obliquely into abscess cavity so as to avoid the area where pointing would occur. *b*: Layers of gauze dressings held by strapping to secure the position of the needle. Needle and dressings are covered with another sterile gauze dressing in between treatments.

*Instillations Following Incision and Suture* (Fig. 2) were used for 4 abscesses, all with large cavities containing 100 to 150 ml. of

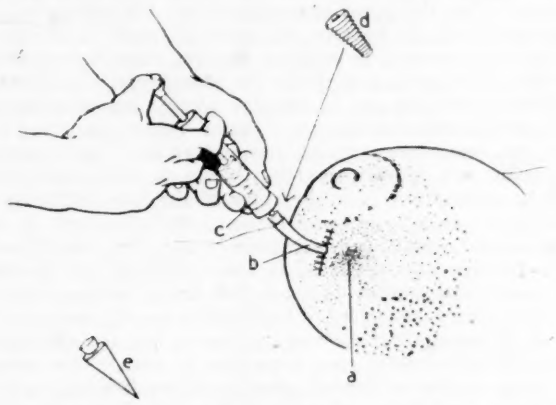


FIG. 2.—Treatment by incision and insertion of drainage-tube. Large abscess tending to point at *a*. *b*: Rubber tubing inserted through incision line, which has been sutured after evacuation of abscess. *c*: Syringe containing penicillin solution—the amount being two-thirds of the pus evacuated or not more than 10 ml. *d*: Adapter for inserting in rubber drainage-tube so as to enable a Record syringe to be used. *e*: Spigot for closing mouth of tube after injection.

pus. Complete evacuation of the cavity required a good opening —away from the area where the abscess was pointing—but this was then sutured round a rubber tube with an internal diameter of about a quarter of an inch (5 mm.). Providing penicillin was instilled, once pus was fully evacuated from a well-localized abscess it did not form in quantity again, and the emptying of the discharge through the tube could then be achieved by gentle pressure. This modified method of drainage was a great deal more satisfactory than aspiration if an abscess contained more than 10 ml. The patients preferred instillations to intramuscular injections or aspirations and injections, for they were almost painless. There was the added advantage that they could be carried out by the nursing staff at more regular intervals than are generally possible with the medical attendant. These abscesses required treatment twice daily for from 4 to 8 days when well localized. Though this method alone cleared up a virulent spreading infection in 15 days, subsequent cases treated with preliminary intramuscular injections till localization had occurred improved more quickly. The choice of local (500 units per ml.) or systemic dose (120,000 units in 24 hours) was governed by the same considerations as have been discussed already, but as administration was twice daily the systemic dose was divided in two, 60,000 units being given at each injection.

The methods used can thus be summed up:

*For the acutely inflamed stage*, intramuscular injections of 15,000 units 3-hourly till localization occurs (120,000 units in 24 hours).

*When fluctuation is detected*, aspiration every 24 hours of all pus, and injection of penicillin solution up to two-thirds of the volume of the pus aspirated, providing this does not exceed 10 ml.

When localization is not complete and full retention of the injection can be ensured, intramuscular injections may be replaced by the injection of the full 24-hour dose of 120,000 units into the abscess cavity. When localization is complete, systemic treatment may be discontinued and, for reasons of economy, a solution whose concentration is 500 units per ml. can be used for injections.

*When the abscesses contain more than 10 ml. of pus*, incision, evacuation, suture, and twice-daily instillations of penicillin solutions following complete expression of pus. The choice of dose is

governed by the same considerations as apply to aspiration, but the systemic dose, as it is given twice daily, can be reduced to 60,000 units.

*Where sinuses exist or are made*, twice-daily expression and instillation by means of a rubber tube or wide-bore blunt-ended needle, the mouth of the sinus being occluded by a collodion dressing in the interval.

Finally, it should be emphasized that complete emptying of the cavity before each instillation is as essential a part of the treatment as it is in the more usual methods of open drainage.

## Discussion

Little work on breast abscesses treated with penicillin has been reported up to date. Complaints in which the risk to life is small have naturally not attracted much attention in the last three years unless directly connected with the prosecution of the war. Yet the social consequences of this malady are considerable, and not least in this category must be placed the inability of mothers to continue suckling their babies when a virulent infection has arisen in the puerperium. Consequently a treatment which can obviate the routine use of stilboestrol has considerable advantages. Fraser (1944) described some not very satisfactory results from local treatment only, and O'Hanlon and MacClancy (1944) seem to have come to no definite conclusions as to the value of the local methods they employed. Hodgkinson and Nelson (1945) reported 24 cases of puerperal mastitis in which three-hourly intramuscular injections for five days appeared to have prevented the formation of breast abscesses in 24 cases, but they considered the use of stilboestrol necessary. Unfortunately no controls were observed simultaneously with this series, and the virulence of infection is known to vary from year to year. This seems to be borne out by our second survey (1945–6), in which no breast abscesses developed in either control or penicillin-treated series when treated early enough by chemotherapy, and the average healing time of the control abscesses was half that in the first survey.

The treatments described in the present paper are by no means unprecedented. One or other, or a combination, have been used in a variety of conditions such as acute suppurative mastoiditis (Florey and Florey, 1943; Macbeth, 1945; Johnson *et al.*, 1945), the suturing of wounds in battle casualties (War Office Report, 1943), acute pyogenic meningitis (Cairns *et al.*, 1944), empyema (Tillet *et al.*, 1944; Fatti *et al.*, 1946), pericarditis (Norman and Ainsworth, 1945), sinusitis (Hauser and Work, 1945), various abscess cavities (Florey and Williams, 1944); Barron and Mansfield, 1944; Noth and Hirshfeld, 1944), osteomyelitis of the mandible (Mowlem, 1944), and in chronic sinuses from osteomyelitis (Florey and Florey, 1943; Robertson, 1944). But the special problem attached to infection in the lactating breast is that of the facility with which multiple loculation occurs, so that the surgeon has been faced with the choice of doing the minimum of damage by incisions which may not drain all loculi completely, or of running the risk of spreading infection by breaking down dividing walls when exploring the extent of the suppuration. Unfortunately, as the controls show, sulphonamide therapy did not give complete protection against this spread, so it is satisfactory to find that it did not occur in any of the cases treated by systemic penicillin.

Now that economy in dosage is not a major consideration there is no reason to suppose that long-continued intramuscular penicillin combined with incision might not eliminate sepsis as satisfactorily as did the method used here of switching over to local administration as soon as it was practicable. The use of vehicles delaying absorption may also rob the intramuscular method of much of its discomfort by reducing injections to once or twice a day. The two great advantages of local treatment, however, are the ability to introduce such relatively enormous concentrations at the focus of infection that there is no need to regulate the dose according to the resistance of any particular staphylococcus and, possibly more important still, both local methods ensure drainage and irrigation of infected surfaces with the minimum of damage to tissues and, in consequence, a much increased rate of healing. In this connexion it must be recognized that the improved rate of healing is by no means due simply to the ability of penicillin to eliminate sepsis. It is, in the average case at least, equally due to the fact that a technique can be adopted that enables healing to take place without the delay caused by the processes of granulation, contraction, and epithelization which the healing of an open wound necessitates.

The technique of finding and of fully aspirating small and sometimes deeply placed abscesses is a matter of skill which requires practice, and is not so easily acquired as that of incision, where anaesthesia enables the surgeon to conduct his exploration with greater ease. The danger in advocating this method of treatment appears to be that less importance is usually attributed to methods of treatment which do not need the panoply of an operating theatre for their execution. If the inexperienced houseman or student is left to carry out aspirations without any preliminary instruction in technique or aseptic precautions (which should be as rigid at the bedside as in the theatre) the method of treatment will undoubtedly cause much suffering and unnecessary damage to surrounding breast tissue. Also, though the continued use of penicillin up to the last time a dressing was required undoubtedly reduced the risks of secondary infection (cf. infection of three controls with haemolytic streptococci), yet the clinical significance of an abscess cavity infected with organisms not susceptible to penicillin is not yet known. For this reason as much care in asepsis should be observed as should have been the rule before this chemotherapeutic agent was available.

## Summary

In 1943–4 two simultaneous series of 18 patients suffering from breast abscesses were treated with present accepted methods and with a combination of intramuscular and local penicillin.

The average healing time in penicillin-treated cases was reduced to half that in controls.

Suppuration was hastened rather than retarded, but ceased more rapidly.

The use of stilboestrol was not necessary, and the mothers were able to continue suckling throughout treatment.

The number of operations was reduced from 22 to 4.

The total number of days during which treatment at the hospital was required was reduced from 661 to 232.

The methods of treatment with penicillin are described in the text, and depend on the preliminary use of intramuscular injections followed by local administration.

### ADDENDUM

A further controlled survey was carried out by two of us (M. A. M. B. and J. S. M.) in the winter and spring of 1945–6. This time penicillin or sulphathiazole was given systemically as a prophylactic measure to all inflamed breasts in the puerperium. Abscesses, when they developed, were treated with similar methods to those described in this paper, but reliance was placed on incision and instillation in 50% of penicillin cases. These results will be published later, but they indicated that early prophylactic use of chemotherapy should reduce considerably the incidence of breast abscesses in the puerperium, and also that the less virulent the prevailing infection the less obvious the benefit accruing from the use of penicillin as compared with sulphathiazole.

These cases were observed and treated entirely at the Central Middlesex County Hospital at the suggestion of the Director, Dr. H. Joules, and owing to the kindness of Mr. T. G. I. James and Mr. J. D. Fergusson, in whose surgical wards some of the cases were nursed and whose responsibility they were. Mr. A. J. Wilson and Mr. H. Hashemian are thanked for their willing help on the surgical side; Dr. J. H. Humphrey and his staff for all the bacteriological examinations; the nursing staff for their enthusiasm and vigilance; and Miss D. M. Barbour for the drawings.

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# CHEMOTHERAPY OF TUBERCULOSIS

## RESEARCH DURING THE PAST 100 YEARS*

BY

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**1935–1946**

PART II

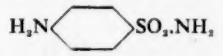
### The Sulphonamides and Sulphones

In 1932 Wells and Long suggested that the stimulus of some new success with other bacterial infections would be needed before the occurrence of any striking advance in the chemotherapy of tuberculosis. And in 1935, after 30 years of progress in the fields of protozoal and spirochaetal infection, but without the chemical mastery of any important general *bacterial* infection in humans, a substantial part of the bacterial front was broken. This, of course, was achieved by the successful use, in experimental streptococcal infection in mice, of azo-dyes containing a sulphonamide ($-SO_2NH_2$) group (Domagk). These were followed, first, by the dye-free sulphanilamide (*p*-aminobenzenesulphonamide, known since 1908), and then by numerous derivatives of the latter, known as the sulphonamides, and by various of the related sulphone ($-SO_2-$) compounds; and many of these synthetic drugs were introduced into medicine (Colebrook and others).

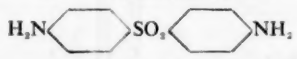
Encouraged by their reasonably high therapeutic index and their efficacy in acute infections, by their diffusibility, and by the presumption that their point of attack in the body was the parasites themselves, investigators tried a number of these sulpha drugs against tubercle bacilli in the test-tube and against experimental infection in animals, and a few of them in patients.

The first drug to be tested was the simplest—i.e., sulphanilamide (Rich and Follis, 1938; Follis and Rich, 1939); the net result of this and other inquiries was that in large and frequent doses some degree of inhibition of the disease in guinea-pigs could be obtained; but neither this compound, nor its derivatives sulphapyridine and sulphathiazole, nor others of the sulphonamide series, offered much hope of usefulness in the clinical sphere. A more promising field was opened up by the introduction, from 1939 onwards, of sulphone compounds into anti-tuberculosis chemotherapeutic experiments; the published data on these agents up to the end of 1944 have been admirably reviewed in detail by Tytler (1944–5), and only the salient aspects of the present position will be mentioned here. The structure of the more important sulphone compounds and, for comparison, that of sulphanilamide is shown in Fig. 2 (modified from Tytler), and it will be seen that three have two phenyl rings linked by the sulphone ($SO_2$) group, while the fourth compound is somewhat different, having a phenyl and a thiazole group linked by the sulphone group.

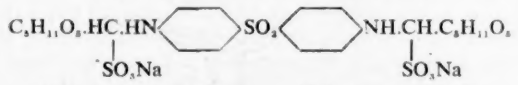
*Sulphanilamide (=para-aminobenzenesulphonamide)*



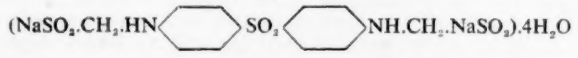
*Diaminodiphenylsulphone*



*Promin (Promanide) (=4, 4'-Diaminodiphenylsulphone-N, N'-dextrose sodium sulphonate)*



*Diazone (=Disodium-formaldehyde-sulphoxylate-diaminodiphenylsulphone)*



*Promizole (=4-Aminophenyl-2'-aminothiazolyl-5'-sulphone)*

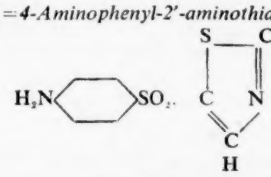


FIG. 2.—Structural formulae of certain sulphones.

The starting-point of the series, diaminodiphenylsulphone, showed some inhibitory effect in infected rabbits and guinea-pigs, but its low water-solubility and high toxicity were bars to its clinical application. The more complex "promin" (promanide) was easily soluble and had a low enough toxicity to warrant extended trials in experimental tuberculosis, which were given by Feldman and his colleagues at the Mayo Clinic and by other groups (see Tytler). The results showed this substance to be a striking inhibitor of the progress of the disease in guinea-pigs (the few observations made in mice—e.g., by Glover in 1945—were much less favourable). But when promin was tested in human pulmonary tuberculosis, although limited benefit was reported by some, the tolerance was found to be considerably lower than in the guinea-pig when the drug was given orally, unpleasant reactions—e.g., a (reversible) anaemia—occurring with some frequency; and while the toxic symptoms were much less evident after parenteral administration, so also was the clinical benefit (Zucker, Pinner, and Hyman, 1942; Heaf *et al.*, 1943; Hinshaw, Pfuetze, and Feldman, 1944; Dancey, Schmidt, and Wilkie, 1944). Experience with "diazone" in experimental tuberculosis in guinea-pigs resembled that with promin (see Tytler), but trials in human pulmonary disease produced conflicting reports, the majority of them unfavourable (Petter and Prenzlau, 1944; Benson and Goodman, 1945; Olson *et al.*, 1945; Pfuetze, 1945; Tice, Sweany, and Davison, 1946; Robitzek *et al.*, 1946). "Promizole" also gave encouraging results in experimental animals in the hands of Feldman, Hinshaw, and Mann (1944), who found it better tolerated by human beings than were the previously mentioned sulphone compounds. However, preliminary clinical trials of this compound in pulmonary tuberculosis have not indicated any marked superiority over promin (Hinshaw, Feldman, and Pfuetze, 1945); it is understood that a fully controlled clinical study is still in progress.

A fair summary of present experience with the sulphone compounds, as judged by those who have worked with them, is as follows. They exercise a deterrent effect on experimental tuberculosis, at least in some animal species, more than any previously tried chemotherapeutic agent; but, while early established lesions may regress and even be resolved, eradication of the virulent infection—a necessary criterion of cure in the acute or subacute disease of the hypersusceptible guinea-pig—is not attained. In man the small numbers and absence of simultaneous matched controls in most trials hitherto reported make assessment difficult, but the results appear nothing like as favourable as those in the guinea-pig; this is because a lower tolerance and risk of objectionable symptoms make adequate dosage difficult to achieve, or because the type of the disease is different, or possibly because the drugs may be altered in the body and become ineffective. At the best, some benefit in recent "exudative" lesions is attributable to these drugs, but there is not a consistent or unequivocal regression of the disease to quiescence or cure. Clinical use of those sulphones at present available seems likely to be limited to external or topical application,* to combination with other agents (e.g., streptomycin†), and to use in other mycobacterial infections (e.g., leprosy). "No definite place has been found for these drugs in treatment of the usual types of tuberculosis" (Hinshaw and Feldman, 1945a).‡

### Other Organic Compounds

Besides the sulpha drugs, a large number of organic chemical compounds have during the past decade been reported to be inhibitory to growth of tubercle bacilli *in vitro*, and a few of

* Conclusion of the Mitchell Lecture delivered before the Royal College of Physicians, London, on July 9, 1946. The first part appeared last week at page 805.

* Tytler and Lapp (1942); Lurie and Stokes (1943); Jarman and Morris (1945); Robin (1945); Grenville-Mathers *et al.* (1946).

† Smith and McClosky (1945a); Smith, McClosky, and Emmart (1946).

‡ For a recent evaluation of the efficacy of the sulphone compounds in experimental and clinical tuberculosis, see Feldman's (1946) Harben Lectures, which are quoted also in the leading article at page 862.

these to be active *in vivo*; a much larger number of *in vitro* positive results remain unpublished. A selected list of reported compounds is given in Table II, grouped according to chemical similarities. Some of them are purely synthetic artificially produced substances with no known counterpart in Nature; others are synthetic compounds related to some natural substance which has served as starting-point of the series; others are themselves of biological origin (these last are placed here rather than in Table III because they fall into convenient chemical groupings, whereas in Table III a provisional grouping by species of origin is adopted).

TABLE II.—*Organic Chemical Compounds Active against* M. tuberculosis in vitro, *or against Tuberculous Infection* in vivo, *grouped according to Chemical Similarities (Recent Publications)*

| Agent (and Reference) | *In vitro** | Experimental Animals† | Man† |
|---|---|---|---|
| *(a) Sulpha Drugs* | | | |
| Sulphanilamide[1] | + | + | – |
| Sulphapyridine[1] | + | ± | 0 |
| Sulphathiazole[1] | + | ± | 0 |
| Sulphadiazine[1 2] | + | ± | 0 |
| Further sulphonamides[2 23] | + | – or 0 | 0 |
| Diaminodiphenylsulphone[1] | + | + | 0 |
| Promin[1] | + | + | ± |
| Diazone[1] | ? | + | ± |
| Promizole[1] | ? | + | ? |
| Further sulphone-compounds[3 4] | + | + | 0 |
| *(b) Fatty Acids and Derivatives* | | | |
| Chaulmoogra derivatives[5 6 7 24] | + | ± | ? |
| Synthetic alicyclic acids[5] | + | ? | 0 |
| Branched-chain fatty acids and derivatives[6 7] | + | ? | 0 |
| Dialkyl succinic acid derivatives[8] | + | 0 | 0 |
| Unsaturated long-chain fatty acids[10 11] | + | 0 | 0 |
| Saturated long-chain fatty acids and esters[9 11 12] | + | + | ? |
| Fatty acid–dye compounds[12] | ? | ± | 0 |
| *(c) Aromatic Compounds* | | | |
| Benzophenone and allied compounds[14] | + | – | 0 |
| Naphthoquinone derivatives[15 22 25] | + | 0 | 0 |
| Naphthalene derivatives; amino- and nitro-compounds and aldehydes[25] | + | 0 | 0 |
| Iodobenzoic and iodosalicylic acids and other aromatic compounds[6 26] | + | + | 0 |
| *p*-aminosalicylic acid[17] | + | ? | ? |
| Halogenated phenyl ethers[24] | + | 0 | 0 |
| Thymol[18] | ? | + | ? |
| 4-*n*-alkylresorcinols[19] | + | 0 | 0 |
| Diethyl-stilboestrol[20] | + | 0 | 0 |
| *(d) Dyes* | | | |
| Acridine derivatives[21 25] | + | – or 0 | 0 |
| Indulin[23] | + | 0 | 0 |
| Various dyes[21 31] | + | – | 0 |
| *(e) Miscellaneous* | | | |
| Synthetic detergents[11] | + | 0 | 0 |
| Amido-compounds of α-furancarbonic acid[24] | + | + | 0 |
| 5-nitro-2-furaldehyde semicarbazone[28] | + | 0 | 0 |
| Urea[28] | + | 0 | 0 |
| Nicotinamide[27] | + | + | 0 |
| Calciferol[28] | 0 | 0 | + |
| Vitamin D and other hydrophenanthrene compounds[29] | + | + | 0 |
| 8-hydroxyquinoline sulphate[30] | + | 0 | 0 |

* Growth-inhibitory or bactericidal effect. † Systemic administration.
+ = Results with the listed substance (or with one or more of the substances in the listed group) reported positive. ± = Results slightly positive, inconclusive or conflicting. – = Results negative. ? = Results not known. 0 = Not tested.

*References.*—[1] See Tytler (1944–5) and text. [2] Smith and Oechsli (1945). [3] Sweaney, Sher, and Kloeck (1946). [4] Lehr and Bloch (1945); Smith and McClosky (1945b); Callomon and Raiziss (1946). [5] Emmart (1946). [6] Küster and Wagner-Jauregg (1944). [7] Prigge (1940, 1941); Buu-Hoï and Ratsimamanga (1942); Wagner-Jauregg (1943). [8] Robinson (1940); Wagner-Jauregg (1942); Buu-Hoï and Ratsimamanga (1944); Buu-Hoï (1945). [9] Barry and McNally (1945). [10] Bergström, Theorell, and Davide (1946). [11] Drea (1944). [12] Negré, Berthelot, Bretey, and Fethke (1945). [13] Bergmann *et al.* (1941). [14] Freedlander (1942, 1944), Feldman, Hinshaw, and Moses (1943). [15] Lloyd and Middlebrook (1944). [16] Saz *et al.* (1941, 1943). [17] Lehmann (1946). [18] McBurney, Cason, and Searcy (1945); Brooks (1946). [19] Drea (1946). [20] Faulkner (1944). [21] Cutting *et al.* (1945). [22] Avery and Ward (1945). [23] Kudrvavtsev (1941). [24] Chpanir and Chertkowa (1944). [25] Dodd (1946). [26] Cummins (1942, 1945); but see Frisk (1946); [27] Chorine (1945); but see Paraf *et al.* (1945). [28] Charpy (1943–6); Dowling and Thomas (1945, 1946); Dowling (1946). [29] Raab (1946). [30] Courmont *et al.* (1936). [31] Willstaedt (1944). [32] Jouin and Buu-Hoï (1946). [33] Frisk (1946). [34] Burger *et al.* (1945). [35] Dubois (1942).

After the sulpha drugs, the most actively investigated compounds have been the chaulmoogra acids and structurally similar synthetic compounds, including synthetic cyclic and branched-chain, many-carboned fatty acids and their derivatives. Renewed interest in this group in tuberculosis springs partly from the historical favourable association of the chaulmoogra acids in the treatment of leprosy, and the earlier consequent research on tuberculosis with these and kindred synthetic products. But work in this field has received new encouragement from the chemical analyses by Anderson and co-workers, extending over the past 20 years, of the lipids of the mycobacteria (see Anderson, 1943). These analyses stimulated the synthesis, by other workers, of lipid-soluble or lipophilic substances that might be expected to penetrate the supposed waxy or fatty "envelope" of the bacillus, or to injure it—e.g., through a surface tension effect. Furthermore, since Anderson's researches revealed the presence in the tubercle bacillus of a series of new branched-chain saturated fatty acids, one of which —phthioic acid—produced tubercle-like local lesions in the guinea-pig, the experiments with various synthetic branched-chain fatty acids made some years before (see above) took on new significance; and the synthesis of fatty acids of similar type to phthioic acid, and so chemically related to a natural bacillary constituent, seemed to offer reasonable promise of blocking some essential biosynthesis (Küster and Wagner-Jauregg, 1944; see also Polgar and Robinson, 1945). Thus there are at least two ideas on the mechanism of growth inhibition—one physico-chemical (fat lysis or penetration) and the other chemical (synthesis-blocking)—guiding current work on the tuberculostatic action of fatty acids and their derivatives. Unfortunately, tests against tuberculosis *in vivo* with selected *in vitro* active substances of this group have so far been little less disappointing than was the earlier work. Moreover, the hypothesis that antibacterial properties can be related to structural similarities with essential metabolites has still to be proved applicable to *M. tuberculosis* (see later). Finally, the results obtained with water-soluble sulphone compounds and with streptomycin, and the fact that the mycobacteria, despite their fatty structure, are more susceptible to water-soluble antiseptics than to fat-soluble compounds, emphasizes that the "lipophilic" approach to the chemotherapy of tuberculosis is not the only one, nor may it be the most fruitful (see discussions by Lehr and Bloch, 1945; Dubos, 1945, pp. 293–4).

The reasons for investigating the aromatic group of compounds, shown in Table II, are diverse. Benzophenone and allied compounds were tested because of their relationship to the sulphones. Napthoquinone derivatives represent an attempt to interfere with the bacterial metabolism through a structural similarity to a hypothetical growth factor or growth stimulant of the vitamin K type. The use of iodobenzoic, iodosalicylic, and *p*-aminosalicylic acids arose from a search for growth inhibitors whose starting-point was the studies of Bernheim (1940, 1941) and others on the increase in oxygen uptake by washed suspensions of tubercle bacilli produced by benzoic and salicylic acids and certain other aromatic compounds; such studies suggested that these or chemically similar substances might play a part in the normal oxidations of the bacilli, and that substituted benzoates and salicylates might interfere with these oxidations and so inhibit growth. The recent renewed interest in dyes has its origin in the promise of the earlier work on tuberculosis by Lewis and others (see above); additional reasons for testing the acridine compounds (including atebrin) are their clinical value in protozoal and bacterial infections, while indulin was used because it was wax-soluble.

In none of this list of compounds has there as yet been strong evidence of efficacy combined with safety in human pulmonary tuberculosis, though with some of them the clinical trials are not completed.* In one non-pulmonary condition, however, a substance has given highly encouraging results in the clinic. The substance is calciferol, whose benefit in lupus vulgaris, when used in high dosage, has been reported by Charpy in France and by Dowling and Thomas in this country, working independently. The results would seem striking and consistent enough to convince without simultaneous controls, and they appear to exceed those obtained in this disease with any previous internally administered remedy. It is to be hoped that further work will confirm and extend these observations, and provide an explanation, e.g., as to whether the calciferol is supplying a deficiency or is acting as a chemotherapeutic agent in the stricter sense. Moreover, while serious toxic reactions have

* A recent Swiss report (Junod, 1946) summarizes work in Japan with the alkaloid cepheranthine (from *Stephania cepherantha* of the family of Menispermaceae). It is active *in vitro* against tubercle bacilli, has low toxicity and is stated to produce arrest, reversal, and often resolution of the lesions of experimental tuberculosis. Improvement is claimed with minute doses in many types of clinical tuberculosis.

not so far been reported as accompanying this treatment, the possibility of calcium deposition in tissues will have to be watched.

### An Antibiotic Age?

Soon after the impetus given to the search for chemotherapeutic agents in tuberculosis by the introduction of sulphonamide drugs in 1935, the bacterial front was further weakened and broken by the successful exploitation of antibiotic substances, none of which had hitherto found an undisputed place in medicine. In 1939 Dubos reported the extraction, from culture filtrates of a spore-forming soil bacillus, of the crude material tyrothricin, from which the crystalline polypeptides gramicidin and tyrocidin were derived; gramicidin was particularly interesting as being active *in vitro* and *in vivo* against certain Gram-positive bacterial species, but its toxicity restricted clinical use to topical application. In 1940–1 the almost ideal chemotherapeutic properties of penicillin—extremely high efficacy in systemic infections by susceptible micro-organisms, little antagonistic action by body constituents, and virtual lack of toxicity—were demonstrated experimentally at the Oxford School of Pathology. These two events stimulated widespread reactivation of this branch of microbiology, and antimicrobial agents were looked for in a multitude of living sources. In this search tuberculosis has figured prominently, particularly as penicillin was found not to inhibit the growth of tubercle bacilli in the test-tube or to retard significantly the development of the disease in experimental animals (Abraham *et al.*, 1941; Smith and Emmart, 1944).

TABLE III.—*Substances from Natural Sources Inhibitory* in vitro *to Growth of* M. tuberculosis, *grouped according to Species of Origin (Recent Publications)*

| Species | Name of Agent | References |
|---|---|---|
| (*a*) Fungi: | | |
| *A. fumigatus* .. | Fumigacin* | Waksman, Horning, and Spencer (1942); Schatz and Waksman (1944) |
| *A. fumigatus* .. | Helvolic acid* | Chain *et al.* (1943); Jennings (1945) |
| *A. fumigatus* .. | Aspergillin | Soltys (1944, 1946) |
| *A. fumigatus* .. | (Unnamed) | Asheshov and Strelitz (1945) |
| *A. flavus* .. .. | Aspergillic acid | Goth (1945) |
| *A. flavus* .. .. | (Unnamed) | Bush *et al.* (1945) |
| *A. clavatus* .. .. | Clavacin† | Waksman, Horning, and Spencer (1942); Schatz and Waksman (1944) |
| *A. ustus* .. .. | Ustin | Kurung (1945); Hogeboom and Craig (1946); Doering *et al.* (1946) |
| *A. albus, niger*, etc. .. | (Unnamed) | Zorzoli (1940) |
| *A.* (unnamed) .. | Mycocidin | Gerber and Gross (1945, 1946) |
| *A.* (unnamed) .. | (Unnamed) | Kallos (1945) |
| *P.* (unnamed) .. | (Unnamed) | Miller and Rekate (1944) |
| *F. javanicum* .. | Javanicin | Arnstein, Cook, and Lacey (1946) |
| *Ch. cochlioides* .. | Chaetomin | Schatz and Waksman (1944); Waksman and Bugie (1944); Geiger, Conn, and Waksman (1944) |
| (*b*) Actinomycetes: | | |
| *S. griseus* .. .. | Streptomycin | Schatz and Waksman (1944); Schatz, Bugie, and Waksman (1944) |
| *S. lavandulae* .. | Streptothricin | Schatz and Waksman (1944); Waksman and Woodruff (1942); Woodruff and Foster (1944) |
| *S. antibioticus* .. | Actinomycin | Schatz and Waksman (1944); Waksman and Woodruff (1941); Waksman and Tishler (1942) |
| *Pr. gardneri* .. .. | Proactinomycin | Florey, Jennings, and Sanders (1945) |
| *Pr. cyaneus* .. .. | Litmocidin | Gause (1946); Brazhnikova (1946) |
| (*c*) Aerobic spore-forming bacteria: | | |
| *B. subtilis* .. .. | Subtilina | Fontes Magarao *et al.* (1944) |
| *B. subtilis* .. .. | Subtilin | Jansen and Hirschmann (1944); Salle and Jann (1945) |
| *B. subtilis* .. .. | Bacillin | Foster and Woodruff (1946) |
| *B. subtilis* .. .. | Eumycin | Johnson and Burdon (1946) |
| *B. licheniformis* .. | Licheniformin | Callow and Hart (1946) |
| (*d*) Non-sporing bacteria: | | |
| *B. larvae* .. .. | (Unnamed) | Holst (1945) |
| Milk streptococcus .. | (Unnamed) | Mattick and Hirsch (1944, 1945); Mattick (1946); cf. Oxford (1944) |
| (*e*) Higher plants: | | |
| *Allium sativum* (garlic) | (Unnamed) | Courmont *et al.* (1937) Rao *et al.* (1946) |
| Onion and garlic .. | Phytoncides | See Tokin (1945) |
| *Clitocybe gigantea* .. (fairy-ring mushroom) | Clitocybine | Hollande (1945) |
| *Plumbago europea* .. | Plumbagol | Saint Rat, Olivier, and Chouteau (1946) |
| Chlorophyll derivatives and related compounds | (Unnamed) | Daly, Heller, and Schneider (1939) |
| *Buellia canescens* (lichen) | Diplolcin | Barry (1946) |

* Helvolic acid is related to, or identical with, fumigacin.
† Clavacin is identical with clavatin from the same species, claviformin from *P. claviforme*, and patulin from *P. patulinum*.
*A.* = *Aspergillus*. *P.* = *Penicillium*. *F.* = *Fusarium*. *Ch.* = *Chaetomium*. *S.* = *Streptomyces*. *Pr.* = *Proactinomyces*. *B.* = *Bacillus*.

In Table III are listed the majority of biological products recently reported as having tuberculostatic or tuberculocidal properties *in vitro*, under the headings of their microbial or other sources. It is already a formidable and rapidly growing collection; perhaps we are entering an antibiotic age in the chemotherapeutic investigation of tuberculosis. A notable feature of the list is the great preponderance of soil micro-organisms, showing the extent to which, in the past few years, soil and medical microbiology have become interconnected in a new way. It is evident also that there is particular concentration of interest around the genera *Aspergillus* and *Streptomyces*, and around the aerobic spore-bearing bacteria of the *B. subtilis* group. The range of activity of the antimicrobial substances produced by the various species listed extends in every instance beyond *M. tuberculosis*, though it is limited and selective; on the other hand, as with other antibiotics, the production tends to be species-specific or even strain-specific (as with streptomycin). In the great majority of the reports listed the *in vitro* evidence rests upon tests with culture fluids or crude concentrated extracts; in relatively few instances has a high degree of purification of the active substance yet been achieved. Names have, however, been conveniently created, even at an early stage of purification, to designate the active agent or agents. Some names—e.g., clytocybine, streptomycin, subtilin, and licheniformin—indicate the genus or species of origin; others are based partly or wholly on the action of the antibiotic—e.g., mycocidin.

In only a few instances among these biological products is there information upon a full trial of efficacy in experimental tuberculous infection, either because investigations have not yet reached this stage, or because the active substance has proved too toxic or is inactivated *in vivo*, or for other reasons. Up to date I am aware of complete reports of such experiments for only two substances—streptothricin and streptomycin.* Since the former showed undesirable toxic effects in laboratory animals and failed, in the dosage practicable, to control experimental tuberculosis in the guinea-pig (Feldman and Hinshaw, 1945a), it has dropped into the background.

### Streptomycin

Streptomycin was discovered in 1944 by Waksman, one of the world's leading authorities on the actinomycetes family, and his colleagues (Schatz, Bugie, and Waksman, 1944; for a review see Waksman and Schatz, 1945). This was the result of a purposeful search among soil micro-organisms for antibiotic agents active against the Gram-negative bacteria and the (Gram-positive) mycobacteria, and suitable for clinical application. The name streptomycin is "derived from the generic designation given to the sporulating and aerial-mycelium-producing group of actinomycetes—namely, *Streptomyces*" (Waksman and Schatz, 1945). The antibiotic was originally found in one particular strain of *Streptomyces griseus*, and, indeed, production has been noted in only a few of the other strains of this species since examined. Streptomycin has been obtained apparently pure. The low toxicity of the purified product for experimental animals (e.g., Molitor *et al.*, 1946; Molitor, 1946), its high power of inhibiting growth *in vitro* of *M. tuberculosis* (Schatz and Waksman, 1944; Emmart, 1945; Youmans, 1945; Youmans and Feldman, 1946), and its survival when introduced into the body, led to extensive tests in experimental tuberculous infection in guinea-pigs (Feldman and Hinshaw, 1944; Feldman, Hinshaw, and Mann, 1945; Smith and McClosky, 1945a) and in mice (Youmans and McCarter, 1945). In guinea-pigs the results of treatment begun simultaneously with, or some weeks after, infection were strikingly better than those with any previous chemotherapeutic agent, and the

* A recent note by Salle and Jann (1946) states that subtilin produces "a definite suppressive effect on the course of experimental tuberculosis in guinea-pigs."

substance was well tolerated. Not only was the development of the disease noticeably inhibited, but arrest and even eradication of established lesions were noted. In mice the effect was not quite so striking, possibly because of a different balance between the doses of drug and infection; definite suppression of the disease process was, however, evident. Owing to shortage of supplies, systematic clinical trials of streptomycin in tuberculosis have so far been mainly confined to its country of origin—the United States—under the supervision of the National Research Council (see Keefer, 1946), and the few published reports are of a preliminary nature (Hinshaw and Feldman, 1945b, 1946—54 miscellaneous cases with limited improvement in some; Cooke *et al.*, 1946—case of tuberculous meningitis with apparent recovery; Figi, Hinshaw, and Feldman, 1946—case of laryngeal tuberculosis with striking improvement; Cook *et al.*, 1946—12 cases of genito-urinary tuberculosis with improvement in some; Baggenstoss, Feldman, and Hinshaw, 1946—histopathology of regressing human lesions).

As seen from this side of the Atlantic, one might summarize the present status of streptomycin in tuberculosis as follows. This antibiotic seems more promising than any previous chemotherapeutic agent. In animals its toxicity is less than, and its effect on experimental infection better than, the best of the sulphone compounds. In man prolonged administration appears to have been free of serious and uncontrollable toxic reactions, though, as in animals, histamine-like responses, evidence of (reversible) renal "irritation," eighth-nerve symptoms, neuritis, and dermatitis have been reported; it seems possible that some of these reactions are due to impurities in certain of the preparations used. The effect on human tuberculosis justifies cautious optimism for certain forms of the disease, but, subject to any very recent information, Waksman's own words of November, 1945, still hold: "Prolonged treatment and studies of many cases are absolute prerequisites for any serious consideration of the efficacy of streptomycin in the treatment of tuberculosis. To date sufficient information has not yet been accumulated" (Waksman and Schatz, 1945). The need for caution has been learned from bitter experience of the past failures with gold, copper, and tuberculin, and from the false promise given by animal experiments with the sulphones. Should streptomycin occupy no more than a temporary place in tuberculosis therapy, the resulting increase in biological and chemical knowledge will nevertheless be very considerable and will assist in further advances.* †

Streptomycin has certain apparently unsatisfactory properties. Like penicillin, it is poorly absorbed from the alimentary canal, so that administration has to be parenteral. Unlike penicillin, it is a base and its activity *in vitro* is reduced by a lowered *p*H, which it might encounter in pus; how far this objection is of practical importance is not decided. A much greater possible disadvantage is that drug resistance is rather easily acquired by the tubercle bacillus and other susceptible micro-organisms, both *in vitro* and *in vivo* (Youmans and Feldman, 1946; Youmans *et al.*, 1946), and this is particularly liable to occur during a prolonged course of treatment. This is one reason why other chemotherapeutic agents would be desirable for use in tuberculosis, even should streptomycin justify present hopes.

### Outlook for the Future

The purpose of this historical review would not be served unless it helped in the assessment of the present position and future prospects. It is therefore relevant to consider some of the difficulties in the path of those who are searching for chemotherapeutic agents in tuberculosis.

In common with all chemical attack on systemic infective disease, the prime consideration is that the chemotherapeutic index of an agent must be reasonably high—i.e., that its effective dose must be substantially lower than the dose toxic to the host. This is where the great majority of prospective agents that are tuberculostatic in the test-tube fall down when tested in the infected body. Other general reasons are failure to disseminate so as to reach the infection site, inactivation by antagonistic substances in the blood or other body constituents, and excessive speed of destruction or excretion; while acquired resistance to the agent by the bacterial parasite is particularly liable to occur when, as in tuberculosis, prolonged administration is required. One general chemotherapeutic aim, however, may have to be modified in the case of human tuberculosis—namely, complete internal disinfection; in fact, when we consider the benign and possibly protective infection which so many of us harbour, the latter may not be necessarily even an essential objective.

There are also difficulties more peculiar to tuberculosis. To be directly inhibitory or lethal to this micro-organism an agent must penetrate the relatively avascular tubercle, enter the possibly vulnerable phagocyte that may enclose the bacillus, and penetrate the "hardy wax-armoured bacillus" itself (Wells and Long, 1932, p. 391); dense fibrotic encapsulation may also constitute a barrier. These difficulties led some workers to see more hope in the indirect attack—by chemical stimulation of the tissue cells around the tubercles, or of the host's defensive mechanisms generally, without contact with the bacilli, as is believed to be the mode of action of heavy metals, certain dyes, etc. Some of these obstacles have, however, probably been overrated. Thus Rich (1945) states: "The tubercle, in spite of its compact, solid appearance, must be permeable to substances in solution, else neither the cells nor the enclosed bacilli could receive the nutritive material necessary for their survival." Actually many diffusible foreign substances will pass from the blood stream into the centres of tubercles and caseous areas—e.g., various vital dyes, iodides, and iron—and some become concentrated therein; penetration of colloidal substances is, of course, much less likely, unless the molecules be small. Rich concludes that many chemotherapeutic substances can reach bacilli in epithelioid cells or in caseous lesions, but that when enclosed in living mononuclear phagocytes the agent must be capable of surviving the internal environment of such cells. If the agent reaches the bacillus, even the reputed waxy or fatty barrier, often supposed to be responsible for the remarkably low susceptibility of mycobacteria to many ordinary chemical antiseptics, seems doubtful in the light of the growth-inhibitory effect, both *in vivo* and *in vitro*, of water-soluble substances such as certain sulphones and streptomycin. Moreover, whether the abundance and variety of the lipids does or does not confer resistance, there is at present no proof that these lipids are organized as a cell capsule or envelope (see Dubos, 1945).

Special difficulties of a technical character also slow the rate of advance. On the biological side, *in vitro* tests are more time-consuming with *M. tuberculosis* than with many bacteria, since the organism grows slowly and uniform inocula and other conditions are not easily attained; recent improvements in media, in the use of submerged culture, etc., may assist (e.g., see Dubos and Davis, 1946). Animal tests also are prolonged, and they need larger amounts of the test substance than do tests in many other infections. The lesions produced in the commonly used experimental animals tend to be acute or subacute, and may differ in other respects from the chronic fibrocaseous lesions of reinfection comprising a large part of adult tuberculosis in man; and, although reinfection can be readily produced in animals, the difficulties of providing a uniform series for chemotherapeutic trials are increased. As to species of animal, the guinea-pig has been the animal of choice for most workers (Feldman and Hinshaw, 1945b), but owing to its lack of natural resistance and comparatively large drug requirements some have turned to the mouse, in spite of its rather atypical non-necrotic lesions (e.g., Glover, 1945; Youmans and McCarter, 1945; Martin, 1946). The chorio-allantoic membrane of the chick embryo is also used, but the tests are not yet on a very firm foundation and some of the techniques are open to criticism. Feldman and Hinshaw (1945b) have made excellent suggestions for standard procedures for chemotherapeutic tests in experimental tuberculosis, with special reference to guinea-pigs. Their criteria for a successful agent are

* For a recent evaluation of the efficacy of streptomycin in experimental tuberculosis, see Feldman (1946).

† A report of 1,000 patients with various infections, treated by streptomycin in the United States, has just appeared (National Research Council, 1946); 87 cases of tuberculosis of the more advanced types are included. Guidance on dosage and administration is given (see also Hinshaw and Herrell, 1946) and toxic manifestations detailed. It is concluded tentatively that streptomycin has a suppressive, though not usually eradicative, action in miliary, laryngeal, meningitic, skin, and renal tuberculosis, and in exudative pulmonary tuberculosis; there is still doubt as to the sequel after discontinuance of treatment. The side-reactions appear more common and somewhat more significant than earlier reports suggest, and certain of them are noted even with apparently pure preparations.

(abbreviated): (1) satisfactory tolerance and absence of serious or irreversible physiological derangements; (2) reversal of established progressive disease to non-progressiveness, resolution, fibrosis, or calcification; (3) eradication of virulent infection; (4) results to be achieved in a reasonable period. In such tests it would be desirable to use "strains of tubercle bacilli whose origin, type, and virulence are known and can, within limits, be guaranteed" (National Tuberculosis Association, 1946).

The preparation of synthetic substances and antibiotic material for *in vivo* trials against experimental tuberculosis requires much initial labour, making *in vitro* "screening" almost a necessity—even though the great majority of agents thus selected as worthy of further attention must be expected to prove ineffective therapeutically. Possibly some more significant screening tests than those that measure growth inhibition will be devised; present alternatives, such as observations on the effect of drugs on oxygen uptake of the bacilli in the resting state (e.g., Bernheim, 1941; Franke and Schillinger, 1944), are of doubtful value in this connexion. Prognostication of the effect in human beings from behaviour of chemotherapeutic agents in experimental tuberculosis provides further misleading possibilities. A good example of lack of correlation between results in test-tube, experimental animal, and man is given by the individual sulphonamides, the best of which are not highly active *in vitro* but give very encouraging results in guinea-pigs, yet have been disappointing clinically. However, few would oppose the principle that new agents of significant toxicity should be administered in human tuberculosis only after promising animal trials. This, of course, does not mean that efficacious agents may not still be first discovered at the clinic or the bedside—such success is shown strikingly in the recent treatment of lupus vulgaris with vitamin D.

The difficulties of evaluating chemotherapeutic trials in man are far greater than in experimental animals. Selection of cases provides a dilemma, for while improvement is most to be expected in early "exudative" lesions unaccompanied by much destruction or fibrosis (as revealed increasingly by mass radiography), these are just the cases that may improve with rest alone or no treatment at all; on the other hand, in chronic fibrocaseous disease the prospect of improvement is doubtful and, if it occurs, may be confused with naturally occurring spontaneous regression. Such considerations call for simultaneous matched controls, an adequate duration of the trial, and an intelligent use of statistics; however, owing to the very obvious obstacles in selecting controls and in giving them inert preparations for some months, most trials have relied instead upon the pre-chemotherapeutic behaviour of the treated patients and on the general clinical experience of the medical observers. Patients and controls should, so far as is possible, form homogeneous groups susceptible of classification, with emphasis in the first instance on bronchopneumonic, "labile," reversible changes. The foregoing difficulties and others inherent in clinical trials, as well as standard procedures to overcome them, are discussed by Hinshaw and Feldman (1944). There is divergence of opinion among experienced workers on some of the points; thus, Zucker, Pinner, and Hyman (1942) and Pinner (1944) hold that, with proper selection of material, preliminary results are obtainable in a brief period, and any positive effect should be obvious enough without controls. Now, if any type of case is suitable for non-controlled observation, it is the "acute" rapidly developing forms of pulmonary disease seen in young adults, and meningeal and some other non-pulmonary forms. One might therefore ask: Will a chemotherapeutic agent produce dramatic enough reversal of progression in such a case to prove that the agent was the determining factor, as has been achieved with penicillin in the absence of direct controls? It is a great deal to ask of it. Or will the ambiguities of "sanocrysin" be repeated? The current clinical trials of streptomycin are relevant to this question, and it should be noted that success has been reported in a few cases of tuberculous meningitis.

## Conclusion

Having thus discussed the history of, and some of the research problems particularly involved in, the search for chemotherapeutic agents in tuberculosis, we can see that two paths are being followed: by way of substances synthesized biologically by various forms of plant life, and by way of products synthesized in the laboratory by the chemist. Along the first path, as with the initial discovery of penicillin, little chemical principle is at present involved in the exploratory phases, which are therefore somewhat empirical. Along the second path the design of synthetic agents is being based on a number of suggestive "leads"; but one fundamental guide is as yet little developed. This is the hypothesis that many antibacterial agents function in virtue of structural similarities to substances that participate in the essential metabolic processes of the bacterial cells ("essential metabolites"), such chemical similarities leading to interference with these processes and so to inhibition of growth. This concept was much strengthened by the study in 1940 of the mutual antagonism between sulphanilamide and the closely related *p*-aminobenzoic acid in the inhibition of streptococci; and it has been used since as a basis for the design of fresh synthetic growth inhibitors for a variety of micro-organisms in which essential metabolites could be defined (e.g., see Knight, 1946). Knowledge of the metabolism of *M. tuberculosis* is, however, still very deficient, this micro-organism seeming able to use the simplest nutrients, to dispense with preformed growth factors, and to synthesize all its essential metabolites—at least after adaptation to the *in vitro* cultural environment in which it is usually studied. Efforts to define its essential metabolites, and to model growth inhibitors on their structure, have so far been confined to lipids, without as yet much result (see above); but further study of the nutritional requirements and metabolic reactions of this micro-organism as a whole may provide a valuable guide to the synthetic design of anti-metabolites that will block some biosynthesis essential to the functioning of its cells.

These two paths along which present work is moving, which originated separately about 50 years ago, can be expected to converge and ultimately to meet; for knowledge of the chemical structure of antibiotic substances may promote laboratory synthesis of active related compounds, while knowledge of the point of interference of such substances may give new information on the essential metabolism of the tubercle bacillus and lead to the purposeful creation of simpler synthetic anti-metabolites.

Should a real measure of success be reached with one or a number of chemotherapeutic agents this is not likely by itself to lead to the eradication of tuberculosis. During the past decade much else has been added to the understanding of this disease and to the ability to control it. Fuller appreciation of the importance of social factors in its incidence and spread, and of the value of social assistance (both financial and re-abling) in consolidating treatment; greater emphasis on the factor of household contact and on earlier diagnosis by means of mass radiography; and the coming to maturity of the various methods of collapse therapy and other surgical procedures: these are among the features of this period in the more favourably placed countries, such as Britain. It is improbable that success in chemotherapy will supersede all the tried and trusted methods of control acquired through the years which are applied to the individual patient, to his family, and to the community. Thus, rest can be expected to remain the foundation of treatment, and surgical methods to be needed in certain types of case; the conditions of life to which the patient returns will surely affect critically the ultimate results of even the most spectacular chemotherapy; and the state of housing and nutrition of the people generally may be expected to continue to influence the secular trend of tuberculosis mortality and incidence. There are in the world perhaps between 10 and 20 million sufferers from active tuberculosis. In order to reduce this inroad on world health we shall probably need most of the reasonable measures—social and economic, preventive and therapeutic—that we possess now or that we can acquire in the future. The attack will remain multiple; the tactics will change.

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# AMBIGUOUS INHIBITION OF STAPHYLOCOCCI BY PENICILLIN INACTIVATED WITH PENICILLINASE

BY

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For some time past penicillinase prepared by the growth of certain strains of *B. subtilis* in broth has been used in this laboratory to inactivate penicillin before testing for sterility. Each batch of penicillinase is assayed by a method devised in the Bacteriological Laboratory of Messrs. Boots Pure Drug Co., Ltd. (personal communication).

A 1:20 dilution of the penicillinase preparation in water is added in ascending quantities to a series of broth tubes each containing 4,000 units of penicillin. These are inoculated with a loopful of a broth culture of a sensitive staphylococcus, and the end-point is read after 40 hours' incubation at 37° C. On one occasion 20,000 units of penicillin was erroneously added to each tube in setting up the assay. On this being realized the penicillinase was diluted 1:4 instead of 1:20, the assumption being that this would give the same result, since the proportion of penicillinase to penicillin in each tube would be the same. However, no growth of staphylococcus occurred in any of the tubes. The assay was then repeated at the normal level of dilution and an end-point was obtained as usual near the middle of the range.

This incident suggested that the ability of staphylococci to grow in broth plus inactivated penicillin is limited to a certain range of concentration of penicillin.

## Experimental Results

It was first shown that failure to grow was not due to a change in *p*H of the broth. The following experiment was then carried out. Serial dilutions of penicillin in broth were made in geometrical progression, beginning with 200,000 units, the last tube containing 781 units. Corresponding dilutions of penicillinase in water were made and 1 ml. of each dilution was added to each corresponding tube of penicillin, so that the proportion of penicillinase to penicillin was the same in each tube. One loopful of staphylococcus broth culture was added to each tube and the series was incubated at 37° C. The tubes were examined first after 24 hours' incubation; growth had occurred only in the tube containing 6,250 units of penicillin. Examination after 40 hours showed growth in the tubes containing 12,500, 3,125, and 1,562 units, but no growth at the four highest dilutions or at the lowest one.

The experiment was then repeated using quantities of penicillin from 100,000 down to 390 units, and on this occasion examination of the tubes was made at hourly intervals. Growth occurred with 6,250 units at less than 19 hours (as it did in a control tube of plain broth), with 12,500 units in 22 hours, with 3,125 units in 24 hours, and with 1,562 units in 30 hours. No growth occurred with 100,000, 50,000, 25,000, 781, or 390 units up to 3 days.

The results of three further experiments are given in Table I.

TABLE I

| Penicillin (Units) | Expt. 1 | Expt. 2 | Expt. 3 |
|---|---|---|---|
| 100,000 .. .. | 0 | 0 | — |
| 50,000 .. .. | 0 | 0 | 0 |
| 25,000 .. .. | 0 | 0 | 0 |
| 12,500 .. .. | 0 | ± 3 days | (4) + 3 days |
| 6,250 .. .. | (2) + 22 hours | (3) + 26 hours | (1) + 21 hours |
| 3,125 .. .. | (1) + 21 ,, | (2) + 24 ,, | (2) + 23 ,, |
| 1,562 .. .. | (3) + 23 ,, | (1) + 22 ,, | (3) + 40 ,, |
| 781 .. .. | (4) + 30 ,, | (4) + 27 ,, | 0 |
| 390 .. .. | 0 | (5) + 40 ,, | 0 |
| 195 .. .. | — | ± 3 days | 0 |
| Control .. .. | + 18 hours | | |

0 = No growth. + = Normal growth. ± = Trace of growth. — = Not done.

It will be seen that growth always begins first in one of the tubes near the middle of the series and spreads outwards through the tubes on either side of the first, though the order is not constant. If the solutions in the high-concentration tubes in which no growth has occurred are diluted with broth to fall within the range of the positive tubes, growth immediately occurs, sometimes being visible in as short a time as three hours after dilution, showing that the penicillin has in fact been inactivated and that the staphylococci have not been killed by the high concentration, for only the original inoculum is still present. Similar results were obtained in other experiments, using three different samples of penicillinase prepared in media other than papain digest broth.

The penicillin used in all the foregoing experiments was manufactured some time ago and was relatively impure, containing 700 to 800 units per mg., assayed against staphylococcus.

Inhibition of growth is not due to anything in the penicillinase; this was shown by making serial dilutions of penicillinase in broth of the same strengths as used in the experiments with penicillin and inoculating with the same staphylococcus. Growth occurred in 18 hours in every tube. It seems evident, therefore, that there is some substance present with the penicillin which, while not affected by penicillinase, in high concentration inhibits the growth of staphylococci.

Confirmation of this hypothesis was obtained by repeating the experiment using purified penicillin, containing 1,600 units per mg., assayed against staphylococcus. An amount of this material containing 100,000 units was diluted serially and each tube was treated with the corresponding quantity of the penicillinase used in previous experiments. The tubes were inoculated from a broth culture of the same staphylococcus. Growth occurred simultaneously in 18 hours with the six highest concentrations, from 100,000 units down to and including 6,250 units. It occurred with 3,125 units in 21 hours, with 1,562 and 781 units in 40 hours, and with 390 units in 3 days. No growth occurred with 195 units up to 5 days. Inhibition at the low end of the scale thus occurs even with pure penicillin.

Three further experiments were done with penicillin from batches having potencies of 1,000, 1,210, and 1,450 units per mg. respectively. The results were as shown in Table II.

TABLE II

| Penicillin (Units) | 1,000 u./mg. | 1,210 u./mg. | 1,450 u./mg. |
|---|---|---|---|
| 100,000 .. .. | (7) ± 3 days | (5) + 3 days | (5) + 42 hours |
| 50,000 .. .. | (3) + 20 hours | (1) + 18 hours + 18 ,, | (1) + 20 ,, |
| 25,000 .. .. | (2) + 18 ,, | | (3) + 24 ,, |
| 12,500 .. .. | (1) + 16 ,, | (2) + 20 hours | (2) + 22 ,, |
| 6,250 .. .. | (4) + 22 ,, | (3) + 24 ,, | (4) + 40 ,, |
| 3,125 .. .. | (5) + 40 ,, | (4) + 40 ,, | (6) + 3 days |
| 1,562 .. .. | (6) + 3 days | 0 | 0 |
| 781 .. .. | 0 | 0 | 0 |
| 390 .. .. | 0 | 0 | 0 |
| 195 .. .. | 0 | 0 | 0 |
| Control .. .. | + 16 hours | | |

It will be seen that, as the potency of the penicillin in units per mg. increases, the first tube to show growth is one step higher in the series. As has been shown, when a potency of 1,600 units per mg. is reached the phenomenon no longer occurs, growth occurring simultaneously with all the higher concentrations.

Further evidence that inhibition with high concentrations of penicillin is due to impurities was obtained by inactivating in the autoclave a solution of penicillin containing 100,000 units in 5 ml., or 20,000 units per ml., and inoculating with one loopful of staphylococcus broth culture. No growth occurred in 7 days, though it occurred in lower concentrations.

Speculation about the nature of any unknown inhibitory substances and their possible therapeutic action is beyond the scope of this paper.

Failure of growth at the very low concentrations of penicillin must be a phenomenon quite distinct from that observed at the other end of the scale and is much more difficult to interpret. In an attempt to elucidate it the following experiment was done:

To four tubes of broth each containing 195 units of penicillin were added the corresponding concentration of penicillinase and one loopful of staphylococcus broth culture. They were incubated for three days; no growth occurred. They were then treated as follows:

Tube 1: excess penicillinase added. Tube 2: one loopful of staphylococcus broth culture added. Tube 3: excess penicillinase and one loopful of staphylococcus broth culture added. Tube 4: no additions. All were incubated at 37° C. with a broth control.

The results were:—Tube 1: +, 24 hours; tube 2: +, 4 hours; tube 3: +, 4 hours; tube 4: 0, 7 days. Control: +, 24 hours.

Tube 1 shows that the original inoculum was still living, but that the original amount of penicillinase added was not sufficient to inactivate the penicillin. Tube 2 indicated that the penicillin had been sufficiently reduced in activity to allow a fresh inoculum to grow; tube 3 is thus redundant, in view of the results with tubes 1 and 2. Tube 4 confirms that the penicillin had not been inactivated by the original addition of penicillinase. The extremely rapid growth in tubes 2 and 3—full growth with maximum turbidity in 4 hours—is difficult to explain. It seems to be analogous to the very rapid growth, noted above, with high concentrations diluted to fall within the critical range of concentration. Both these observations seem to indicate that treatment of penicillin with penicillinase at submaximal levels for several days increases the susceptibility of the medium to growth of staphylococcus when the conditions are altered sufficiently to allow growth to take place. That the alteration is in the medium and not in the inoculum seems clear from tubes 2 and 3, where the inoculum was fresh.

### Discussion

The observations here reported are, apart from any academic interest, of practical importance for sterility-testing of penicillin.

This laboratory is frequently called upon to test for sterility dried penicillin in phials containing up to 1,000,000 units. In the light of the observation here reported it is clear that to make certain of getting growth of sensitive contaminants the final dilution in the test medium should be related to the potency of the sample in units per mg. With potencies of less than 1,000 units per mg. it should be of the order of 1:100. However, with penicillin of recent manufacture, potencies of at least 1,400 units per mg. are usual, and it should not be necessary with such samples to employ volumes of test broth larger than those normally used for sterility testing. Where very low concentrations of penicillin are to be tested for sterility care must be taken to add gross excess of penicillinase, of the order of 10 times the equivalent quantity, whatever the potency of the sample. This does not normally arise in practice.

Apart from the above practical considerations, the phenomenon described is interesting from several points of view. Inhibition by high concentrations suggests that impurities in penicillin exert on staphylococci an inhibitory effect that is not a true penicillin effect, for it does not occur with "pure" penicillin. Inhibition at the low end of the scale is more difficult to understand. It would seem that penicillinase does not act proportionately to its concentration—that the relationship of penicillinase activity to concentration of penicillin is in fact not linear. Consequently the value obtained by the method of assay described holds good only for a limited range of penicillin unitage—round about 4,000 units. The quantitative relationship of penicillinase and penicillin may have a bearing on the generally assumed enzymic action of penicillinase.

The extremely rapid growth of staphylococci (full growth from a single loopful in 3 to 4 hours at 37° C.) after reducing to a normal dilution a concentrated penicillin solution in which growth has so far failed to occur is a most striking phenomenon and difficult to explain. So also is the similar rapid growth in very dilute penicillin in broth after excess penicillinase has been added to a tube in which no growth has so far occurred. Such rapid growth has never previously been observed in this laboratory: it would seem to merit further study.


### Summary

Staphylococci are inhibited by penicillin above a certain concentration, notwithstanding that the penicillin is shown to have been inactivated by penicillinase.

This does not occur with "pure" penicillin, suggesting that the inhibition is due to impurities.

Similar inhibition occurs in penicillin dilutions in broth below a certain concentration. In this instance the inhibition is due to the penicillinase having failed to inactivate.

In both instances, if the penicillin in broth is rendered capable of supporting growth by diluting the high concentrations or by adding excess penicillinase to low concentrations, growth of staphylococci occurs with extraordinary rapidity.

The implications of the observations are discussed from the point of view of sterility-testing of penicillin.


## MESENTERIC OCCLUSION

### A REVIEW OF RECENT METHODS OF TREATMENT, WITH NOTES ON SIX INSTANCES


BY

**H. MORGAN WILLIAMS, M.B., B.S., F.R.C.S.**


Mesenteric occlusion is one of the rarer abdominal disasters and one that is very difficult to diagnose pre-operatively, very difficult to treat, and recovery from which is most exceptional. Having had experience of six cases in the last four years, with three recoveries, my interest was aroused and I was stimulated to consult the literature.

The occlusion may be arterial or venous, and may be thrombotic or embolic. Venous thrombosis is usually a complication of a septic process within the peritoneum. Arterial emboli may arise from cardiac vegetations, whereas arterial thrombi are likely in blood disorders—e.g., purpura. The arterial architecture is very important. The small intestine is supplied entirely from branches of the superior mesenteric artery, dividing into a series of arcades. There is no marginal artery such as is found in the large intestine. When an occlusion occurs in the area of the small intestine it has been suggested by Litten (1875) that a violent spastic contraction occurs from the ligament of Treitz to the middle of the transverse colon. The last case described below is difficult to explain on an arterio-anatomical basis. The symptoms may be acute or subacute: constant pain is a regular feature, with only moderate or ill-defined tenderness. Vomiting is more likely if the upper reaches of the alimentary tract are involved. Constipation or diarrhoea may occur.

Diagnosis may be facilitated in subacute cases by a plain skiagram, where gas is seen as far as the splenic flexure and a barium enema reveals no obstruction. Prognosis is always grave, but patients have lived many years after operation.

Treatment must be decided after the state of affairs has been assessed at laparotomy. The appearances found vary considerably: the bowel affected may be black, and profuse haemorrhagic exudate may be present; in others a deeper cyanotic colour is seen, with ecchymoses and less heavily blood-stained exudate. If the affected length of bowel is not too great and the patient's condition is good enough, a resection can be undertaken and anastomosis performed. Ficarra (1944) describes fifteen cases, three of which were cured by resection; Atkins (1937) reports recovery by resection, exteriorization, and subse-

quent closure; D'Abreu and Humble (1946) describe cases where small intestine was removed successfully, and careful administration of heparin subsequently is emphasized as an important factor. In all cases of cure resection had been performed, except in a case of lymphatic leukaemia (Murrey Scott and Lissimore, 1944), where the only treatment was dicoumarol 0.05 g. on alternate days. In three of the cases quoted below it will be seen that recovery occurred without resection; in only one case was heparin used. The routine followed (after dismissing the possibility or advisability of resection) was to institute an intravenous glucose-saline drip and, when vomiting threatened, to aspirate the gastric contents through a Ryle's tube. Except in one slight case (No. 4) this was maintained for ten days, and then the bowels were opened by pituitrin 0.5 ml. and a turpentine enema.

## Case Histories

*Case 1.*—Miss C., aged 80. The patient was an arteriosclerotic subject with some evidence of myocardial failure. She had diffuse abdominal pain for two days, constipation, and vomiting; and there was distension without localized tenderness. Laparotomy showed cyanosis and distension of almost the whole of the small intestine. Nothing could be done, and the abdomen was closed. The patient died a few hours later.

*Case 2.*—Captain P., aged 76, a stout man retired from seafaring life, had two days' abdominal pain—not localized; vomiting; and constipation. A few days before this he had developed a slight purpura. Examination showed a dry tongue and distended abdomen, with no localizing features; his general condition was good. The diagnosis was mesenteric occlusion. Laparotomy brought to light a mesenteric occlusion affecting about five feet (1.5 m.) of small intestine. Resection was immediately decided upon and rapidly performed with an end-to-end anastomosis. The patient's condition on return to bed was good; but he never recovered consciousness, dying twenty-four hours later. Evidence suggested death from cerebral thrombosis.

*Case 3.*—Mrs. C., aged 58, had two days' history of right-sided abdominal pain with profuse diarrhoea; temperature 99° F. (37.2° C.), pulse 92. Her previous health had been good. Examination showed a dry tongue, and the abdomen slightly distended, with marked tenderness in the right iliac fossa. The diagnosis was appendicitis. Operation revealed a normal appendix, but the bowel was cyanosed from a point just distal to the caecum to the upper part of the descending colon. This was considered too extensive to resect, and nothing was done. The clot was found in the right colic artery. The patient was put on an intravenous drip, which was continued for seven days, and then a rectal drip for three days. Complete starvation by mouth was ordered. At the end of ten days the patient—to my surprise being still alive—was given an injection of pituitrin 0.5 ml. and a turpentine enema, with an excellent faecal result and the passage of flatus. For several days things went smoothly, the bowels acted on alternate days with enemas, and she took a gradually increasing amount of food by mouth. On the sixteenth day abdominal pain and tenderness were felt just above the caecum; her temperature rose to 100° F. (37.8° C.) and a slow perforation with localization was suspected. She was put on penicillin for four days, when the temperature subsided and the abdominal pain abated. She vomited several times. At the end of a week she seemed out of danger. She took light invalid solid diet, and the bowels responded to liquid paraffin and cascara. The tender mass gradually decreased in size, and after a month she went home. The patient remains well after six months.

*Case 4.*—Mr. H., aged 70. Hitherto a fit man requiring no medical attention, he had two days' history of abdominal pain, vomiting, and constipation. Examination showed a dirty tongue, slight distension of the abdomen, and localized tenderness over the right iliac fossa. Blood pressure was 230/120. A diagnosis of appendicitis was made. At operation the appendix was found normal; there was free blood in the peritoneal cavity, and ecchymoses of the caecum and a short length of ascending colon pointed to local occlusion of a mesenteric vessel. The abdomen was closed and an intravenous drip set up. Heparin was used in the drip, which was continued for three days, and complete starvation by mouth was insisted upon. Pituitrin 0.5 ml. and a turpentine enema resulted in a good bowel movement and passage of flatus. Light food by mouth was now taken, and the patient rose from bed on the eleventh day. He made normal progress as from a laparotomy.

*Case 5.*—Miss T., aged 74. This case is most interesting, as the patient had two attacks. The first ended in complete recovery (following laparotomy) for thirteen months. At the second attack there was partial recovery, but death resulted from a subsidiary cause. Originally she complained of abdominal pain with vomiting for four days. There was vague tenderness in the centre of the abdomen, but no disturbance of temperature or pulse, and the bowels responded to enemas. Laparotomy disclosed an extensive occlusion affecting the upper two-thirds of the small intestine. Nothing operative could be done, so the abdomen was closed and an intravenous drip established. No food or drink by mouth was allowed, and a Ryle's tube was left *in situ* for several days, with frequent aspirations of stomach contents. This was continued for ten days. Pituitrin 0.5 ml. and a turpentine enema were given, and faeces and flatus were passed. The Ryle's tube was withdrawn and the drip discontinued. Liquids by mouth, and then solids, were allowed. Gradually recovery ensued; the abdominal distension slowly subsided, and the patient was as well as she had been for years.

After thirteen months the symptoms returned and were an exact repetition of the previous attack: vague abdominal pain with persistent vomiting. She went to a nursing home, and, being confident of the diagnosis, I did not advise laparotomy. She was treated as before with a Ryle's tube (which sometimes withdrew up to four pints (2.3 litres) of faecal matter), and an intravenous drip (later replaced by a rectal drip owing to difficulty with her available veins). After ten days the pituitrin and a turpentine enema produced a good result. She began to take fluids by mouth, but this time her convalescence was much impeded by vomiting and tremendous distension of the abdomen. Unfortunately she developed an ulcerative stomatitis with cervical lymphadenitis and parotitis. She was given penicillin, which controlled the accompanying fever, and pus was aspirated from the abscess that formed in the submaxillary region. She made a gallant fight for seven weeks, and seemed to be definitely better, with no vomiting for the last two weeks. Then she suddenly died from heart failure, apparently due to toxaemia. Post-mortem examination showed the same area of the bowel to have been affected—the upper two-thirds of the small intestine. It was still distended to twice the normal calibre, and the walls were cyanotic and thin. No accurate estimate of the state of the vessel could be obtained as examination was very difficult.

## Discussion

In two cases (Nos. 3 and 4) the area affected was the large intestine, and one can understand how an anastomosis could be established by collateral vessels. In Case 5 a great length of small intestine was involved; on both occasions of occlusion recovery took place, although the intestine as seen at necropsy was still poor in appearance and performance. How did the length of bowel recover? In both the large-intestine cases the diagnosis made beforehand was appendicitis, presumably because of the localized tenderness over the distended caecum. In Case 2 and Case 5 mesenteric occlusion was diagnosed before laparotomy.

The choice of treatment at laparotomy would seem to be along the following lines. In large-intestine cases, if the intestine is not too gravely affected, expectant treatment is justified even if resection be thought practicable. In small-intestine cases resection should be carried out unless the amount of intestine involved is too great or the patient's condition makes it impossible. As much as 19 ft. (5.85 m.) of small intestine has been successfully removed.

## Summary

The case reports of five patients with mesenteric occlusion are discussed. The possibility of the success of expectant treatment, particularly when the large intestine is affected, is emphasized.

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To secure the full use of the services of all available specialists, in view of the needs of the National Health Service, the Secretary of State for Scotland has informed the principal hospital authorities concerned that he is willing to meet the cost of additional full-time specialists at salaries up to £1,000. The approval of the Scottish Department of Health is to be obtained in each case. The Secretary of State will expect hospital boards to co-operate with the post-graduate organization of the appropriate university in making an appointment. The Department's approval will be given on the understanding that each appointment and the conditions attached to it are subject to review once the National Health Service is established. These arrangements are a development of the scheme set up by the Scottish universities and the Department of Health, under which ex-Service doctors training as specialists are appointed to special training posts in hospitals with salaries paid by the Department.

# REITER'S DISEASE

BY

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The recent article by Jackson and the case report by Wrigley on the syndrome known as Reiter's disease (*B.M.J.*, 1946, **2**, 197, 199) will no doubt have stimulated clinicians to review in retrospect a number of hitherto obscure cases. It will be remembered that the disease is characterized by the triad of non-specific urethritis, arthritis, and conjunctivitis, with the occasional accompaniment of keratodermia blennorrhagica, haematuria, and diarrhoea.

A. M. H. Gray in his article on keratodermia blennorrhagica (*Med. Annu.*, 1941) quotes Epstein as associating this disease with inflammation of the joints and eyes and discussing its relation to psoriatic arthritis, believing the two conditions to be distinct; for, whereas psoriasis more usually appears on knees and elbows and sometimes on trunk and extremities, the lesions of keratodermia are entirely confined to soles and palms. This view, he goes on to point out, is further confirmed by Taylor, who describes the condition as one secondary to severe polyarthritis and posterior urethritis of gonococcal origin. Gray further quotes Combes, Dietrich, and Cohen, who, after minutely describing the skin lesions, point out that the arthritis is not of the more usual monarticular variety seen in gonococcal infections but a polyarthritis which involves chiefly knees, ankles, wrists, and acromio-clavicular joints, and which, further, shows less than the usual periarticular oedema and inflammation.

Reports of cases of Reiter's disease are so few that the occurrence of a case which in retrospect fits closely into the clinical picture would appear to justify its publication.

## Case Report

The patient was an English soldier of 41 who was admitted to Hillingdon County Hospital on Dec. 12, 1945, with the following history. Until the beginning of August, 1945, he had been in perfect health and had not—and in this he is to be believed—run the risk of venereal infection. About Aug. 1, while serving in Norway, he developed an acute conjunctivitis, which became purulent within a short time and for which he received local treatment. He was repatriated on Sept. 6 and admitted to another hospital, where the conjunctivitis, still acute, was treated with penicillin drops. A few days after his admission an acute purulent urethral discharge made its appearance; he had never had such a thing before. Repeated examinations of the discharge failed to reveal the presence of gonococci, and serological examinations were likewise negative. Parenteral penicillin resulted in complete disappearance of the discharge in five days; nor was there any recurrence. Three months after the onset of the conjunctivitis the patient developed an intraocular haemorrhage in the right eye, and a few days later iritis in the same eye. The iritis ran its usual course of ten to twelve weeks, and settled down only to recur after his admission to this hospital, as will be described later.

Four months after the original conjunctivitis joint symptoms were first complained of, the ankles, knees, and shoulders becoming stiff but exhibiting no signs of redness or swelling. Not until two weeks later was the first sign of swelling noted—in the second left metacarpo-phalangeal joint—and the temperature for the first time was found to be above normal. At approximately the same time that joint symptoms first became manifest a scaly eruption of the soles was observed.

On Dec. 12 the patient was admitted to this hospital, and his condition was then as follows. He was somewhat thin, and arms and legs showed wasting consistent with a prolonged stay in bed from subacute arthritis. The ankles were swollen and painful and only slightly red; the knees were stiff and painful but not swollen; the left shoulder and elbow were in a similar condition, and the only other affected joint—the second left metacarpo-phalangeal—was swollen, slightly red, and very painful. There was a thick scaly eruption of both soles, which was misdiagnosed as psoriasis in spite of the absence of other skin lesions, and under the free edges of the nails of some of the fingers was a collection of dry cheesy material. The conjunctivae were slightly inflamed, but there was no crusting of the lids. The right eye showed signs of old iritis, with a fixed irregular pupil and posterior synechiae. There was no urethral discharge and the urine was normal. Examination of the other systems was negative, but the E.S.R. was 106, and the gonococcal complement-fixation test and Wassermann reaction were both negative. The temperature on admission was normal.

A course of "myocrisine" was started on Dec. 31, to which the response was satisfactory in that, the day after each injection, increased pain was experienced in the affected joints, and a slow but steady improvement in mobility and pain took place so that two months later the patient was once more able to walk. Since then there has been no relapse, and on Sept. 13, 1946, the only sign of trouble is a persistence of some swelling and stiffness of the metacarpo-phalangeal joint.

A recurrence of iritis of the right eye took place on Jan. 31, 1946, resolving in the course of ten weeks with the help of hot bathing and instillations of atropine, "protargol," and other eye drops. On May 8 the left eye developed iritis, which resolved in about eight weeks. At the time of the last examination, on Sept. 13, there was no sign of inflammation in either eye, although synechiae persisted.

The scaly eruption of the soles continued *pari passu* with the joint lesions, and at one time it caused considerable distress from the foul odour arising from the layers of dead skin. Treatment with Condy's-fluid baths and the use of a detergent ointment resulted in some improvement, but as the joints cleared so did the skin, and now there is no trace of it on the soles; under three nails on the hands there is a small collection of dry cheesy material.

During the first twelve weeks after admission he ran a slight irregular temperature—never above 98.8° F. (37.1° C.).

The patient has recently been readmitted to have an operation for hammer toe, and, apart from the few signs mentioned above, he now shows no trace of the illness which started just over a year ago. Weight and colour have returned, and he looks forward to being able to restart work soon.

## Comment

The interest in this case lies in the exhibition of all the symptoms of the disease except for the diarrhoea and haematuria, as well as in the sequence in which the symptoms made their appearance—conjunctivitis, urethritis, then polyarthritis and keratodermia coincidently, with recurrent iritis as a concomitant. In view of the complete clearance of symptoms and signs as reported in other cases, it is doubtful if the treatment given in this case had any effect if we except only the rapid clearance of the urethral discharge with penicillin.

I have to thank Dr. W. Arklay Steel, medical director of Hillingdon County Hospital, for permission to publish this report.

# Medical Memoranda

## Perineal Suture in Obstetric Practice

In my practice the patient is generally delivered lying in the left lateral position, even when delivery is instrumental, as it is easier when one is single-handed. In this position, satisfactory as it is for the delivery, visualization and suture of a perineal laceration are difficult, since the raw edges tend to fall together and it is far from easy to locate the upper end of the vaginal part of the tear. In an attempt to solve this difficulty the method described below has been evolved. The basis of the technique is insertion of two deep tension silkworm-gut sutures placed longitudinally on each side of the perineum before delivery of the child. The insertion of these sutures is made near the end of the second stage in such cases as (1) where perineal laceration may be expected; (2) where episiotomy is necessary; and (3) where there is marked stretching of the perineum.

### TECHNIQUE

Two semi-curved Hagedorn needles are threaded with strong silkworm gut. The area round the perineum is thoroughly sterilized by washing the part with biniodide solution. The index and middle fingers of the left hand are inserted into the lower third of the vagina, and then separated in fanlike manner in order to protect the presenting part and also to draw the perineum forwards. The needle is inserted through the perineal skin about 1/4 in. (6 mm.) from the midline and 1/4 in. from the muco-cutaneous junction, the point passing deeply into and through the vaginal mucosa. The needle then travels within the vaginal cavity, re-entering the deep tissues 2 in. (5 cm.) nearer the vaginal vault and emerging through the perineal skin 1/2 in. (1.25 cm.) above and lateral to the anus. Within the vagina the suture lies on the mucous membrane and the lower end traverses the muscles surrounding the anus. The suture is repeated on the other side of the perineum, and both stitches are secured by clamping the free ends of the silkworm gut with artery forceps. With these stitches in position the delivery of the child is completed. Should a laceration have taken place or an episiotomy been necessary the inspection of the wound and the estimation of its extent can easily be carried out by traction on the two lateral

sutures. Access to the depth of the wound is made easy, and the insertion of catgut sutures for the repair of the vaginal mucosa and deep muscles made relatively accurate. After the catgut sutures have been inserted and tied the skin is closed by tying the free ends of the silkworm sutures.

### COMMENTARY

The value of this technique lies in the fact that (1) it renders the single-handed repair of an episiotomy or laceration moderately easy; (2) the sutures are in place should laceration occur; (3) if there has been no laceration or episiotomy, but considerable stretching of the parts has caused injury to the deeper tissues, these separated deep tissues are held together by the sutures.

I am aware that self-retaining retractors have been devised to facilitate perineal repair. These are more satisfactory when stitching is done with the patient in the dorsal position, but their use also implies introduction of instruments into a fresh wound in that area.

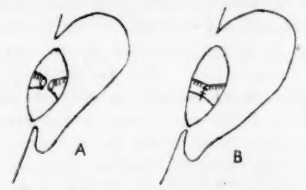
Broomhill, Selkirk. D. CHARTERIS GRAHAM, M.B., Ch.B.

## Transverse Rupture of External Auditory Meatus

Recent reports in these columns of minor but interesting and unusual injuries prompt me to record a case of traumatic transverse rupture of the external auditory meatus. I have not previously heard or read of this injury. In the present case the nature of the causal trauma was no doubt a shearing force transverse to the line of the meatus.

### CASE HISTORY

A girl aged 9 was knocked down by a motor car. In the casualty department a small and superficial cut behind the right auricle was cleansed and sutured, and the patient was admitted to the ward for observation in case of intracranial injury. No evidence of serious injury was found, however, but blood was seen to be escaping from the right auditory meatus. Examination with the auriscope revealed a complete annular laceration of the skin tube at a depth of 5 mm. from the bottom of the concha. The inner part of the meatus had retracted and was visible only as a small circular skin edge, round which lay the damaged supporting cartilage. Repair was undertaken under general anaesthesia. The cut behind the auricle was reopened, excised, and extended, and then deepened anteriorly so as to expose the divided ends of the meatus (see Fig. A). After excision of all tags of tissue, including loose pieces of cartilage, the ends of the skin-cartilage tube were found to fit neatly together and were sutured with five fine catgut stitches, passing through skin and subcutaneous tissue (Fig. B). Sulphanilamide powder was




Showing the external meatus (A) before and (B) after repair.

inserted, and the retro-auricular wound closed with a small rubber dam drain through its lower end. A flavine-in-glycerin pack was inserted into the now continuous meatus. Healing took place rapidly and without sepsis, and a slight tendency to stenosis was subsequently treated by repeated dilatation.

DOUGLAS R. K. REID, M.D., F.R.C.S.,
Dunedin Hospital, New Zealand. Surgical Registrar and Tutor.

## A Case of Reiter's Disease

Practically all the articles on Reiter's disease during the past three years have appeared in American or Canadian medical journals. I understand from colleagues that cases with symptoms that correspond to the recognized syndrome of polyarthritis, urethritis, and conjunctivitis are not rare in this country, especially in V.D. departments, but as very few cases have been recorded the following typical case may be of interest. As an allergic reaction to bacillary dysentery may be the cause in some cases (Reiter's original case was associated with diarrhoea and blood in the stools), it is interesting to note that this patient had not had diarrhoea in the year preceding the onset of his illness, during which time he had been in this country.

### CASE HISTORY

The patient, an Englishman aged 34, served in various parts of the Middle East from November, 1940, to January, 1945, when he returned home. He had three mild attacks of diarrhoea during that time, the last in 1944. No attack lasted more than three days, there was no blood in the stools, and he was not admitted to hospital. He believes he had conjunctivitis in both eyes in December, 1944, which persisted for about two weeks. A dental abscess developed in December, 1945, and a tooth was removed on Feb. 5, 1946. In January, 1946, he experienced pain in the left side of the back, and a week later there was a slight urethral discharge, but no dysuria or frequency. The following day he had conjunctivitis of both eyes. Two urethral smears showed many pus cells and some mixed organisms, but no epithelial cells or Neisserian organisms. He denied any chance of exposure to venereal infection before the onset of his illness. Non-gonococcal urethritis was diagnosed, and a course of sulphathiazole (27 g. in all) was given. Ten days after the onset of the urethral discharge his right ankle became swollen, and a few hours later there was swelling and pain in the left knee. Next his back became stiff, and pain and stiffness in the shoulders, elbows, and fingers began; none of these latter joints became swollen. He was admitted to hospital on Feb. 9, two weeks after the onset of the urethral discharge.

On examination he was seen to be a well-developed adult male. He had severe bilateral purulent conjunctivitis. There was some pain and stiffness in the lumbar region on movement. The right ankle was red, hot, and swollen. There was some limitation of flexion of the right knee but no swelling. Movements of the arm-joints were full, but he could not flex the fingers of the right hand owing to pain. His oral temperature was 101° F. (38.3° C), pulse rate 100, and respirations were below 20; his pulse was regular. The blood pressure was 130/85. The throat was clean, and the teeth showed no obvious sepsis. There were no abnormally enlarged glands and no sign of abnormality in the chest or abdomen. Smears from the eye swabs showed a few polymorph pus cells but no organisms, and cultures were sterile. The blood count showed: haemoglobin, 14.8 g. %; R.B.C., 4,640,000; W.B.C., 6,800 (polymorphs 66%, lymphocytes 34%). He was given sod. sal. and sod. bicarb., āā, 30 gr. (2 g.) four-hourly, and the eyes were treated with irrigations and atropine instillations. On Feb. 11 the B.S.R. was 75 mm. per hour. The urine contained a fair amount of pus: a stained deposit showed a few Gram-positive diplococci. He continued to run a mild pyrexia of 99 to 100° F. (37.2–37.8° C.). On Feb. 22 the prostatic smear was crowded with polymorph and epithelial cells. Only a very few staphylococci were seen in the fresh smears. The urethral discharge was very scanty by this time. Next day he was given 200,000 units of penicillin in beeswax and peanut oil. He had no further urethral discharge after this. During the next two days there was a definite improvement in the eye condition, but the temperature and joint pains remained unaltered. Sodium salicylate was stopped on Feb. 28. On March 1 the B.S.R. was 74 mm. per hour.

The temperature had not settled by March 9, and he was still getting pains in the left lower back and across the shoulders and some pain and stiffness in the legs. Penicillin, 30,000 units intramuscularly, was given, followed by 15,000 units three-hourly. This was continued for six days, when a total of 645,000 units had been given. The temperature was not affected and the pulse rate remained at between 80 and 100. On March 13 the blood showed Hb, 13.3 g. %; R.B.C., 3,720,000; W.B.C., 8,100 (polymorphs 66%, lymphocytes 29%, monocytes 4%, eosinophils 1%). Mist. ferri ammon. cit. was given and he was sent to a convalescent home on the 15th to remain in bed there. The temperature became more settled about the end of March, and early in April it was mainly normal, with occasional rises to 99° F. (37.2° C.). The pulse was steady, between 80 and 90. While at the convalescent home he had toothache.

The patient returned to hospital on April 15 complaining of pain in the right shoulder, down the right arm, and in the right ankle. He still had conjunctival injection after sleeping. His blood count now was: Hb, 16.3 g. %; R.B.C., 5,200,000; W.B.C., 7,500. Wassermann, Kahn, and gonococcal complement-fixation tests were negative. B.S.R. 36 mm. Urine: pus cells two per field, no organisms seen. Examination showed slight injection of the left conjunctiva. Right ankle: full movements, but skin reddened over the outer part. He still complained of pain in the right ankle, but skiagrams revealed nothing abnormal. On April 22 he complained of some tenderness in the left ankle and slight puffiness. He still had toothache, and a skiagram on the 26th showed some bone infection near the root of $\text{—}|^{34}$. On May 2 $^{2}\text{—}|^{345}_{34}$ were extracted under gas. B.S.R. 30 mm.

On June 9, four months after admission, he was feeling better, but still had occasional joint pains and slight conjunctival injection in the morning. B.S.R. 9 mm. Urine: no albumin, no pus, blood, or casts, no organisms seen. He started to get up, and sulphacetamide ointment was applied locally to the eyes, without improvement. He was discharged from hospital on June 28. The temperature was normal, rising very occasionally to 99° F. (37.2° C.), the pulse rate between 70 and 90, and the B.S.R. 8 mm.

He was seen on three occasions as an out-patient, the last time on Oct. 26—nine months after the onset of his illness. He still had some mild aching in the joints, especially of the right arm and right ankle, and also occasional pains in the lumbar region and the back of the neck, which varied with the weather. A skiagram of the right ankle showed no evidence of structural change in the joint. He had no urinary symptoms, but was still getting slight injection of the eyes on waking. B.S.R. was 8 mm. per hour.

I wish to thank Dr. Ronald McD. Cairns, who was in charge of the case, and at whose suggestion I have written it up, for permission to publish this report.

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# Reviews

## DIGITALIS

*Digitalis and other Cardiotonic Drugs.* By Eli Rodin Movitt. (Pp. 204; illustrated. 30s.) New York and London: Oxford University Press. 1946.

The use of digitalis is attracting increasing attention in the United States at the present time to judge from the appearance of a second monograph within a few months of a first. This second book contains a frontispiece showing the beneficial effect of "cedilanid" on the *x*-ray appearance of the chest of a patient with rheumatic heart disease and congestive heart failure. Cedilanid is the name given to lanatoside C, which is a glycoside obtained from digitalis lanata, and which on further breakdown (loss of glucose and of an acetyl group) gives rise to digoxin. In part Dr. Movitt's book reads like a benediction on cedilanid, and a suspicious mind might think the book represents successful propaganda on behalf of this substance. Cedilanid is discussed with enthusiasm in 24 pages, while digoxin is discussed in 3½ pages, in which it receives no bouquets whatever.

A foreword is written by William Dock, who, together with Tainter, demonstrated the action of digitalis in causing constriction of the hepatic vein in normal dogs as a result of which there is a fall of venous pressure. The author is at pains to state that Dock and Tainter do not consider that the action of digitalis in congestive failure is to be explained by this action. Nevertheless, increasing interest is being shown, especially by clinical workers, in the possibility that in congestive failure the action of digitalis is exerted not on the heart itself but on the vessels elsewhere. Thus there appears to be no doubt from the work of McMichael and Sharpey-Schafer, which confirms the earlier observations of Steward and Cohn and also of Rytand, that in the normal human subject digitalis causes a fall in cardiac output and a fall in right auricular pressure. The fall in cardiac output must be a consequence of the fall in right auricular pressure, and this in its turn must be the consequence of some change in an organ or in a vascular area away from the heart. In the patient with heart failure, however, digitalis causes the same change of pressure in the right auricle, but this is attended by an increase in cardiac output, and therefore both effects are more likely due to an improvement of the heart's action. It is very easy to demonstrate the increased force of contraction of the failing heart when digitalis is administered to the heart-lung preparation of the dog. It is clear, however, that it will be some time before agreement is reached on this subject.

Dr. Movitt's book deals not only with digitalis but also with the glycosides of strophanthus and squill. The literature has been widely studied and the exposition is interesting.

## PEPTIC ULCER

*Peptic Ulcer.* Its Diagnosis and Treatment. By I. W. Held, M.D., F.A.C.P., and A. Allen Goldbloom, M.D., F.A.C.P. (Pp. 382; illustrated. [$6.50.) Illinois: Charles C. Thomas. 1946.

This book is written by two New York consulting physicians. It might well have been built up out of a series of lectures to students or graduates, and it gives a rather static picture of ulcer. Successive chapters deal with aetiology, pathology, diagnosis, and treatment. The various complications of peptic ulcer and the surgical treatment are dealt with fully. There are many excellent reproductions of *x*-ray photographs but little about the gastroscopic appearances of peptic ulcer in activity and healing. The survey of the material tends to be compendious rather than critical. The problems of diet and treatment with alkalis are not handled in a scientific manner, whereas a number of bizarre and unorthodox remedies are mentioned. The authors tell us very little about the natural history of peptic ulcer and there is no statistical information about the effects of different treatments on its course. Hardly anything is said about the secular changes in incidence of peptic ulcer or the social pathology and psychology of the disease. An immense amount of good British work on incidence, haemorrhage, perforation, psychological factors, differential diagnosis of ulcer from nervous dyspepsia, alkaline treatment, and a variety of other topics has escaped the notice of the authors. The book is extremely well produced and printed, and is reasonably priced, but it is not one we can recommend. It is twenty years behind the times for readers in this country in both matter and approach.

## NATIONAL HEALTH INSURANCE

*National Health Insurance in Great Britain, 1911–1946.* By R. W. Harris. (Pp. 224. 12s. 6d.). London: George Allen and Unwin Ltd.

Anything on this subject coming from the pen of Mr. R. W. Harris demands respect. As a young Civil Servant he was in at the beginning of our National Health Insurance legislation and took a very active part in its early administrative stages. When he retired from the Service he continued his practical interest in it as chairman of the London Medical Services Subcommittee. He is well known as joint author of *Medical Insurance Practice*, which for many years has been the valued guide of all insurance practitioners. His present book covers a much wider field, for it surveys the whole of National Health Insurance as it at present exists—its sources, its inception, its evolution, its anomalies and difficulties, its successes and failures. His facts can always be relied on, and his opinions are always temperate and founded on knowledge and practical experience. It is a pity that the war prevented the publication of this book six years ago, for it is possible that a study of it by those responsible for the imminent developments in National Health Insurance might have learned from it some useful lessons in how not to do it—lessons which were painfully learned by Mr. Lloyd George and his staff.

Every aspect of the system is clearly described and analysed. Part I deals with "National Insurance"; Part II with "National Health." Our system was "made in Germany," but we were by no means the first country to follow the example set by Germany in 1893. Mr. Harris shows, however, that Germany owed much to the pioneer work of British friendly societies, and that the benefits they had gradually built up for their members grew out of the desire of the British working man to provide a decent burial free from any help from the Poor Law. Mr. Harris clearly shows how the decision of Mr. Lloyd George to use the friendly societies and trade unions in the administration of our system led to many complications and anomalies, all of which are examined in detail. He comes to the conclusion that in spite of these, as an organized scheme for the payment of money during sickness and disablement it has been "an unqualified success." He does not feel so sure about "its value as a contribution to the general health and welfare of the community." His reasons for this reservation are very similar to those which have been presented, without success, by the B.M.A. to one Government after another. This part of the book has a bearing on the prospects of the extended National Health Insurance now before the country. Mr. Harris has at any rate the satisfaction of knowing that finance and health are to be separated administratively, as he has advocated for some years. If this book has, through no fault of its author, been deprived of its opportunity of full usefulness in influencing a further stage of National Health Insurance it can at any rate claim to be a valuable contribution to the social history of our country.

## AN AMIABLE AUTOCRAT

*Men, Medicine, and Myself.* By S. Vere Pearson, M.D., M.R.C.P. (Pp. 254. 12s. 6d.) London: Museum Press Ltd. 1946.

It would be unfair for anyone to complain that Dr. Vere Pearson's "apologia pro vita sua" is too full of his political prepossessions or of tuberculosis "shop," for the title of it gives everyone due warning of what to expect. To his friends (and everyone who has met him is, or wants to be, one of them) this frank record of his career in medicine, of his achievements at Mundesley Sanatorium, of his interest in agriculture, sociology, oecology, and so forth, reveals him just as they have known him. It is no inconsistency that first made him an ardent Labour Party propagandist (though he admits he never believed in Socialism) and then led him to disillusion and dislike of all politicians—red, pink, or blue—but rather the reaction of a generous nature compelled first of all by his sympathies with under-dogs to champion their cause, and then by his intellect to realize that some remedies are worse than the social diseases for which they are prescribed.

To his colleagues in the profession, especially his contemporaries, the first chapters, which deal with his early days in medicine, his adoption of tuberculosis as a specialty in consequence of developing that disease, and his pioneer work in collapse therapy in this country, are of greater interest than the later ones, which are rather for enlightenment of the general public as to hygiene and social problems, especially those connected with tuberculosis. There are many well-told anecdotes about eminent physicians of the older generation, and much that enables those who can look back on the medical world of forty-five years ago to see more clearly than they otherwise might do the problems of that time and the evolution of methods for solving them.

When the author deals with the problems of medical education as he sees them to-day, his suggestions are perhaps more debatable, though there will be many to agree with his comments on what is often called "penny in the slot" diagnosis of disease. At any rate he has, we may be sure, thoroughly enjoyed "getting things off his chest"—which after all is to be expected of an expert in pulmonary lesions. At Mundesley he confesses that he finds it necessary to be an absolute autocrat—though doubtless he does not regard his patients as under-dogs—and it would certainly be interesting to know what his nickname is, to learn whether he has carried there the old sobriquet of student days, "Severe" Pearson, given to him by antinomy as being the very last adjective that could justly attach to him, or whether anyone has thought to call him "Mr. Chips." It is typical of his reticent modesty that he nowhere mentions that he was a rowing blue at Cambridge and a member of one of the outstanding crews of those days.

## Notes on Books

*All About the Deaf* is a handbook compiled by the National Institute for the Deaf (105, Gower Street, W.C.1: 3s. or 3s. 3d. post free). Its forerunner was first issued over twenty years ago. Since that time there has been a great stirring of the public conscience in regard to the needs of the deaf and of the deafened, and this is illustrated in the number of agencies which now exist for their relief and help, and the variety of forms which such assistance takes. The legal provisions which affect the deaf, the education of the deaf and dumb, the work of local authorities on behalf of the deaf community, the recent developments in hearing aids—these and many other matters are set out so as to convey the maximum amount of information in the most concise form.

*The Cardio-pulmonal Function during Pregnancy*, by Dr. G. WIDLUND, Supplement I to *Acta obs. gynae scand. XXV.*: (Uppsala) is a symposium valuable both for its original studies and for its comprehensive bibliography of some 300 papers in which there is incidentally, no doubt as a consequence of war, a noticeable shortage of references to recent English and American contributions. The pregnant woman is shown to have an increased oxygen consumption, increased vital capacity, and slight increase in pulse rate and blood pressure, and the material will allow a considered evaluation of the techniques of pneumothorax and pneumoperitoneum. The painstaking study is presented in English and gives one more proof of the liberality of Swedish medical education.

## Preparations and Appliances

### CHIP GRAFTS IN THE NECK OF THE FEMUR

Mr. F. P. FITZGERALD, F.R.C.S.I., Harley Street, London, W.1, writes:

One of the great difficulties in the treatment of fractures of the neck of the femur by nailing is the delay before union is complete. Some years ago, in an attempt to overcome this, I treated a fairly large series of cases by grafting the neck of the femur with the fibula, alone and reinforced with a nail (*Lancet*, 1943). The results were disappointing. Recently I have utilized chip grafts from the ilium, so far with complete success, and a detailed account of the cases is in preparation. The following is an account of the method and instrument used.

The instrument, or chip graft gun (see Fig. 1), resembles a large trochar and calibrated cannula with a funnel (A and B), and a special hollow auger bit to fit the cannula (C). Two guide wires are placed in the neck of the femur. A nail is threaded over the upper one in the usual way. The auger-bit is fitted into the cannula, and threaded over the lower guide wire. By rotating the handle a hole is bored in the femoral neck along the guide wire, and the instrument forced into the bone to the required depth, as noted on the calibrated cannula. The auger-

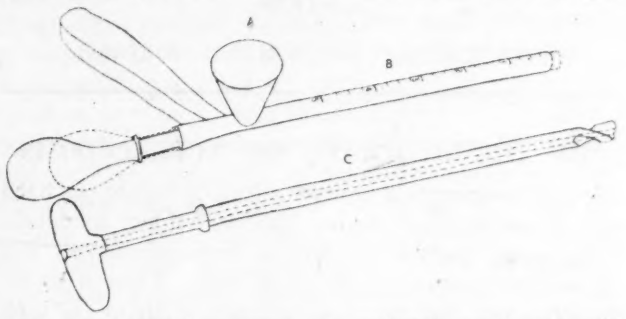


FIG. 1.—A, funnel or hopper. B, graduated cannula with solid plunger or trochar in place. C, hollow auger-bit which fits the cannula.

bit is then withdrawn, leaving the cannula in place. Finely cut chips are then dropped into the hopper, and packed home through the cannula with the solid plunger or trochar. The cannula is gradually withdrawn as the space becomes filled with chips, and the instrument is removed when the cavity has been filled to the outer cortex of the bone. The wound is then closed in the usual way.

The instrument can also be used for extra-articular arthrodesis of the hip-joint.

FIG. 2.—A case one month after operation.

The broken lines in Fig. 2 show the position of the chip grafts.

Nurses' Salaries Committee Notes nos. 12 and 13 have been issued by the Ministry of Health (price 4d. and 2d. respectively from H.M. Stationery Office). The former is concerned with (a) female hospital nurses, (b) male hospital nurses, (c) public health nurses, (d) ex-Service male student nurses, (e) trained nurses: title to increments in respect of service in the Forces, and (f) post-certificate leave for public health nurses; and the latter with nurses variously employed in the public health services. The recommended revised scales have effect from Jan. 1, 1946.

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## THE CHEMOTHERAPY OF TUBERCULOSIS

The ever-widening field in which chemotherapy has attained clinical success leaves the few hitherto resistant conditions in increasing prominence. Among these, tuberculosis and virus diseases stand out above all others. There is so far scarcely a hint that the viruses are susceptible to any such attack, and nothing that we know of their properties and behaviour encourages belief to the contrary. In tuberculosis, on the other hand, much has already been done, and those who care to take stock of the situation will find ample material in the Mitchell Lecture by P. D'Arcy Hart, the full text of which is given in the present and preceding issues of this *Journal*. It can rarely have happened that two such notable contributions to the study of a single subject should be made in the same month as this and the Harben Lectures[1] delivered a few days later by W. H. Feldman, of the Mayo Clinic. Both lecturers trace the history of their subject and recognize that present-day developments date from the observation of Rich and Follis in 1938 that the progress of experimental tuberculosis in the guinea-pig is retarded by the administration of sulphanilamide. Thence sprang a series of studies embracing further sulphonamides and, later, sulphones, revealing increasing degrees of therapeutic efficacy in the experimental disease. The origins of antibiotic therapy may be said to go much farther back—more than thirty years ago Vaudremer in Paris treated over 200 cases of tuberculosis with a substance derived from an *Aspergillus*—but the effective study of such substances dates only from the recognition of penicillin as a true chemotherapeutic agent in 1940. Development on these lines has led us to streptomycin, the only antibiotic so far to receive adequate trial, both experimental and clinical, in the treatment of tuberculosis.

Feldman's contribution is notable for its very full description of experimental study, in which he has taken a major personal part. That properly conducted therapeutic trials in animals should precede any sort of clinical trial will be generally recognized: what "properly conducted" means is not so well understood. Feldman lays down rules for therapeutic tests in guinea-pigs which might with advantage be generally followed. The strain of tubercle bacillus used for producing the infection should preferably be a "classical" one available to other workers. There should be two sets of control animals—untreated, and treated by some other agent of known degree of efficacy, such as one of the sulphones. The severity of the test can be varied by varying the quantity of tubercle bacilli with which the animal is inoculated, but still more by extending the period which elapses between inoculation and the beginning of treatment. The agent has the best chance if administration is begun at once. The severity of the test can be progressively increased by delaying treatment for any period up to seven weeks, by which time disease is well advanced. This may be verified by a tuberculin test or even by liver biopsy before treatment is started. Feldman also provides a scheme for assessing the extent of disease in numerical terms, taking into account not only gross but histological findings. The extreme test of freedom from disease of such an organ as the spleen is the inoculation with it of another animal. What sulphonamides and sulphones on the one hand, and streptomycin on the other, will do is clearly set forth in his paper, both diagrammatically in terms of gross lesions and numerically in terms of his system of scoring. The sulphones, notably promin, do much: their "suppressive" effect—meaning arrest of the progress of the disease without actual elimination of the organism—is prolonged, even when treatment is delayed for six weeks; but they do not eradicate the infection, and the disease progresses when treatment is stopped. Streptomycin, on the other hand, when administration was begun at the same time, appears actually to have cured a large proportion of animals: in 52% there was "no discernible tuberculosis either gross or microscopic"; some had ceased to react to tuberculin when finally killed, and in 7 out of 9 such negative reactors the spleen was non-infective to other guinea-pigs. Similar results were obtained with many strains of tubercle bacilli, and with the bovine as well as the human type. They were also obtained, when treatment was begun 23 days after inoculation, regardless of whether the daily dose of 4 mg. was given in four, two, or one daily injections, or even in doubled quantities daily during alternate weeks. Whether this surprising result means that streptomycin can be given infrequently to patients instead of according to the usual 3-hourly schedule is a question which is not discussed. Feldman also records, in tabular form, the results of treating 75 tuberculous patients with streptomycin. The most striking item in this list is the survival of 4 out of 7 patients with meningitis. In other categories assessment is naturally more difficult, though a majority in most are judged to have shown a favourable response.

We must turn to our own pages and the wider outlook of D'Arcy Hart for a more comprehensive account of what is going on now, and for a far-sighted appreciation of future possibilities. For those not fully apprised of the scope of modern tuberculo-chemotherapeutic work his list of chemical compounds, with a statement of their activity —*in vitro*, in the experimental, and in the human disease—against *Myco tuberculosis* will be astonishing. These compounds fall into no fewer than five categories, and although of very unequal merit they embody two strictly rational lines of approach: an active compound may conceivably either enter and attack the organism by virtue of lipoid-solubility, or it may block an essential synthesis. The latter approach appears to be the more promising, but in the absence of more clearly defined knowledge of the metabolism of *Myco. tuberculosis* there is no certainty that a substance acting in this way exists. Another equally formidable list of potential chemotherapeutic agents, their activity in many cases being still largely unexplored, is that of the antibiotics. Here we are on purely empirical ground, and D'Arcy Hart's prophecy—that the approach from this direction and from the study of synthetic chemical compounds

[1] *J. R. Inst. Pub. Hlth.*, 1946, **9**, 267, 297, 343.

backed by some hypothesis as to their possible mode of action will ultimately meet—is perhaps looking rather a long way into the future. Apart from a few agents derived from such peculiar sources as garlic, a lichen, toadstools, and streptococci, substances inhibiting the growth of the tubercle bacillus have been obtained chiefly from *Aspergilli, Actinomycetes,* and *Bacilli.* Some of these are known to be too toxic for clinical use; others have not yet been tested *in vivo*; and hundreds of others doubtless remain to be identified. Certainly no other agent is yet known to approach streptomycin in therapeutic efficacy; on the other hand, streptomycin is not the ideal beyond which no one may hope to go. Its clinical efficacy cannot be finally assessed, but it is certainly not absolute. Some toxic effects are now being observed after heavy dosage; and the fact that in some patients tubercle bacilli recovered after a course of treatment have exhibited a thousandfold increase in their resistance to streptomycin must be a bad augury.

The discussion of the future outlook with which the lecture concludes emphasizes some of the difficulties with which the work contends. One is only comparative—the very leisurely pace at which everything proceeds where the tubercle bacillus is concerned: *in vitro* and *in vivo* experiments take weeks and months, whereas with most other bacteria they are a matter of hours and days. More formidable is the series of barriers, in the tissues and perhaps in the tubercle bacillus itself, which any effective agent must penetrate. It is encouraging to hear the view expressed that these difficulties have perhaps been exaggerated. On the other hand, the difference between the experimental disease in the guinea-pig and its more chronic form in man is distinctly to the disadvantage of the latter. It is perhaps noteworthy in this connexion that the success of antibacterial chemotherapy as we know it now, though its two agents are unrelated, varies in each case directly with the acuteness of the disease, and with the rate of multiplication of the infecting organism. Chronic infections, whether because the organism is multiplying less actively or because it is protected by the surrounding tissue reaction, are more resistant both to sulphonamides and to penicillin. If it is legitimate to apply this finding to the field of tuberculo-chemotherapy the result is not encouraging. On the other hand it is, fortunately, reasonable to hope that in a semi-resistant animal such as man treatment which does not produce complete sterilization of the lesion may yet achieve a large measure of success.

## RESEARCH IN TROPICAL MEDICINE

Few engaged in medical research or practice in the Tropics but will acknowledge a debt of gratitude to the many activities and helpful publications of the Liverpool School of Tropical Medicine. Founded in 1898, and now not far from its fiftieth anniversary, the School has been second to none in the wealth of research it has carried out or in the extent and usefulness of its publications. A record of what the School has achieved during the six years of war, recently published, gives evidence of its valuable work during this critical period. Under the late Prof. Warrington Yorke's energetic organization the Liverpool School has provided courses of instruction in tropical medicine for medical officers of the Army and Navy attended by approximately 2,000 officers. Additional classes were given at the request of the War Office for R.A.M.C. pathologists, and at the request of the Chief Surgeon of the United States Army for members of the U.S. Army Medical Corps waiting to be drafted to tropical areas. Publication of the *Annals* was continued under considerable difficulties, 175 papers appearing from 127 different authors between September, 1939, and December, 1945. In the six years of the war the staff of the School contributed more than 90 papers to scientific journals besides many secret reports for Government Departments and Committees. In the wards over 1,000 cases of amoebic dysentery were treated. In West Africa the staff of the Sir Alfred Jones Laboratory at Freetown, at the request of the Sierra Leone Government, took over the greatly expanded pathological service at this large wartime naval and shipping centre.

Members of the Liverpool School staff have as individuals and as representatives of the School served on many committees and bodies concerned with the progress of the war effort. Prof. Yorke was appointed a vice-president of the Anglo-Soviet Medical Union in 1941, and shortly before his death went to the United States on a commission on the vital matter of improving the prospects of adequate supplies of mepacrine—in which he was brilliantly successful. In 1940 and again in 1944 Prof. D. B. Blacklock at the request of the Colonial Office returned to West Africa to investigate and advise upon the menacing malaria situation in the West Coast ports. Researches in many urgent matters relating to the war have been extensively conducted. Undoubtedly the most striking event in this respect has been the discovery of the antimalarial drug paludrine, which promises to solve some of the most difficult features of drug prophylaxis in malaria. During the war experience showed that mepacrine as a prophylactic was capable of changing the whole outlook on malaria prevention in a tropical campaign. But even mepacrine was not a completely satisfactory drug, and search for the ideal drug has been actively carried out in the war years both in this country and in America. Among compounds submitted for test by Imperial Chemical Industries there was discovered at the Liverpool School in 1942 an entirely new range of chemical substances having a therapeutic action on the malarial infection of birds, and early in 1943 one of these drugs—No. 2666—was tested on human cases. This and the compound No. 3502 were, however, not very effective, but further compounds of the series were successively tried, including Nos. 3349 and 4430, which were about as effective as quinine or mepacrine, until finally No. 4888 or paludrine was reached. Tested in human malaria by Adams, Maegraith, and their co-workers, this was found not only to arrest acute attacks of both benign and malignant tertian but to be devoid of any side-effects. Judging from the results reported elsewhere obtained by Fairley in Australia, it would appear that paludrine is eminently suitable for prophylactic use, since it does not, like mepacrine, produce yellow coloration, is extremely non-toxic, and even taken one day in the week appears to be an effective prophylactic.

Among other important researches that have been made are investigations of the action of different diamidines in kala-azar, trypanosomiasis, and babesia infections, on an epidemic of sleeping sickness in which these drugs were successfully used, on acquired drug resistance, and on the treatment of scabies and its control by the use of 5% tetmosol soap. The report includes a tribute to the memory of Warrington Yorke, whose outstanding contributions to chemotherapy have brought fame to himself and the School. It is gratifying to read that response to the appeal for the Warrington Yorke Memorial Fund had up to the end of 1945 led to contributions and promises under deed of covenant of £46,530 towards the capital sum of £60,000 asked for.

## THE CLOSED MIND

What has this country come to when a Medical Officer of Health is compelled to dismiss from hospitals under his control nurses and doctors because they will not join trade unions—and this at a time when hospital beds have to remain empty because there are not enough nurses to go round? Yet this is what has happened at Willesden. The matron, the deputy matron, 36 nurses, and one doctor of Willesden Municipal Hospital, and the matron, resident medical officer, and 11 certified State midwives at Willesden Council's maternity hospital, Kingsbury, were last week given one month's notice. This notice of dismissal was, according to the accompanying letter from the Medical Officer of Health for Willesden, "in view of the fact that you have not complied with the Council's resolution regarding membership of a trade union." Seventy nurses and a number of probationers at Walthamstow Council's two hospitals have just been notified that they must join a recognized trade union or organization: this notification was tactfully handed to them along with their pay packets. According to a statement in the Press, the Medical Officer of Health for Walthamstow said: "We have given the nursing staff a list of nine professional organizations which they may join, such as the Royal College of Nursing and Nalgo." Heston and Isleworth Borough Council decided at its last meeting "that all employees shall be members of their respective trade unions, provided that such unions be affiliated to the T.U.C. or eligible for affiliation thereto." The Gateshead Council has also decreed that all its employees should become "members of an appropriate trade union," and Gateshead teachers are up in arms about it. These fresh bungles of Bumbledom are fortunate because their crass folly has drawn on them the wholesome publicity of a Press which still remains free. The next scene in "Insanity Fair" will, no doubt, be the refusal of the authorities to admit patients to hospitals unless they have a trade union ticket.

At Willesden, the sister tutor and deputy matron had been serving at the hospital for 24 years and the night sister for 26 years. Two of the staff nurses had given their faithful service, one for 20 and the other for 28 years. Yet these women were given a month's notice because they would not conform to a requirement which had no relation to their function or capacity as nurses who care for the sick. It is no exaggeration of language to describe such treatment as outrageous. They have, along with their fellow nurses, stoutly refused to accept a position which is intolerable to them as free individuals practising a humane and self-sacrificing profession. Miss Ward, matron of one of the Willesden hospitals, said in a statement to the Press: "The staff will do their duty, but I cannot guarantee, with the feeling there is among the staff, that they will all remain after this. . . . The staff are more determined than ever that they will not join a union." The stand taken by the Willesden nurses will, it is suggested, compel the borough's General Purposes Committee to withdraw the notices of dismissal, and it is believed that the Committee will recognize the Royal College of Nursing.

Though Willesden may wriggle out of the ludicrous situation in which it has placed itself there still remains unsettled the issue of compulsion by local authorities on their medical and nursing employees to join a trade union or recognized professional organization. Dr. F. R. Ellis stated in a letter published in the *Supplement* of November 23 that in answering an advertisement in the *Journal* for a full-time medical officer at a borough council—it was Willesden—he received with his application form a notice which included this statement:

"That trade union membership be a condition of employment of all persons continuing in or entering the service of the Council, and that present employees who are not members of a trade union be advised of this decision and given a reasonable time—i.e., by Nov. 1, 1946—in which to join a trade union."

At a meeting of the Council of the B.M.A. on November 6, 1946, it was explained that local authorities were requiring employees (1) to be members of a trade union or professional association, (2) to be members of a trade union, but accepting membership of "Nalgo" as satisfying the condition, or (3) to belong to a trade union affiliated to the T.U.C. The Association immediately appointed a Committee to investigate the position, and the matter will be discussed once more at the next meeting of Council. In the meanwhile, the Secretary of the B.M.A. has stated that "In the view of the B.M.A., no doctor should be required to join any body, the B.M.A. or other. Membership should be a voluntary act. Wherever a local authority imposes a condition of trade union membership the Association will advise the profession not to apply for appointments under such an authority." A statement of the attitude of the B.M.A. in relation to the position in Willesden and other areas, and the steps it proposes to take, will be made after the meeting of the Council on Dec. 11.

The medical profession is to-day independent, and the majority of its members are free to choose their way of life and livelihood. When officialdom exercises its petty tyrannies we can resist with effect and safeguard the professional liberties of doctors in whole-time employment. But when the whole profession is in the employment of the State where will be the safeguards? Willesden is a disturbing sign of the modern menace—the "closed mind."

## PENICILLIN IN ACUTE MASTITIS

There is probably no malady which causes more suffering to the mother than acute mastitis at a critical time in her life and that of her baby. Treatment has so far proved unsatisfactory, especially in the case of the mother who is in her own home, suffering perhaps from severe pain, struggling to keep the household going and to look after a young infant. Even in hospital the various methods of treatment in current use have proved far from ideal. For these reasons, and because treatment with the sulphonamides has proved disappointing, treatment with penicillin opens up great possibilities. The primary infection appears to be almost invariably due to *Staph. aureus*, an organism not generally very sensitive to sulphonamides but sensitive to penicillin.

In this issue of the *Journal* Lady Florey, Mr. MacVine, and Miss Bigby describe the treatment of breast abscesses with penicillin, giving the results in 18 cases and comparing them with those of 16 control cases treated with sulphonamides. It was found that in the penicillin-treated cases there was a significant reduction in the duration of pyrexia and suppuration and a decrease in the healing time. Penicillin was given at first systemically by intramuscular injections of 15,000 Oxford units every three hours. As soon as fluctuation was detected, or when the abscess appeared to have localized and was small, pus was aspirated and penicillin injected into the abscess cavity under local analgesia—120,000 units in some cases and 500 units in others. It was found that under treatment pus gradually disappeared and was replaced by sero-sanguineous exudate. A culture was made from this fluid, and if *Staph. aureus* was absent no further treatment was necessary. It was found that 4 to 7 daily local injections were required. Sinuses developed very readily in penicillin-treated cases, and penicillin was instilled along the track of the sinus after expression of pus or, in other cases, by a needle inserted until a sinus formed and then along the track of this sinus. Abscesses containing more than 10 ml. of pus were incised and drained, and penicillin was instilled twice daily after expression of pus. The importance of complete expression or aspiration of pus before injection or instillation of penicillin is emphasized. Suckling is continued, and the authors consider the administration of stilboestrol unnecessary.

In a recent article in this *Journal*[1] Mary D. Taylor and Stanley Way describe the use of penicillin in 10 cases of acute puerperal mastitis. Treatment was started early, the indications being pyrexia associated with flushing and hardening of the breast, or in some cases pyrexia with pain in the breast. Systemic injections were given, but details of dosage are not stated, only the total doses, which varied from 300,000 to 1,050,000 units. Suppuration occurred in only one case, and all were cured in seven days, 6 out of the 10 patients being cured in three days or less. These authors recommend that suckling be temporarily discontinued if it causes discomfort, and that in these cases a small dose of stilboestrol (not more than 1 mg. in 24 hours) be given. The breasts are kept empty.

Penicillin is now within reach of every practitioner in adequate quantities, and it seems that it should prove very valuable in treating acute mastitis and in preventing and treating breast abscesses. Treatment should begin as soon as possible and penicillin should be given in adequate doses. In domiciliary practice three-hourly injections are difficult, but good results can be obtained by giving two or three injections of 100,000 units or more per day. Use of the oily solution prolongs the effect. Taylor and Way recommend stilboestrol where there is flushing and discomfort, but advise only a small dose. Lady Florey and her colleagues are opposed to this, but they do not say why: perhaps it is because they do not wish to inhibit lactation. It has been found, however, that if suckling is continued stilboestrol in small doses does not generally inhibit the production of milk, though it does often help to diminish vascular engorgement and discomfort.

A partial solution has been found for a problem which has long proved difficult and distressing for those entrusted with the care of puerperal patients and mothers who are feeding their babies. It is to be hoped that the use of penicillin will not only diminish suffering from mastitis but will help to increase the incidence of breast-feeding.

1 *British Medical Journal*, 1946, **2**, 731.

## PENICILLIN SYNTHESIS

The ending of the official secrecy with which the laboratory synthesis of penicillin has hitherto been invested compels some attention, even if the achievement proves of no more practical importance than as an entry in future textbooks of biochemistry. Penicillin was first synthesized more than two years ago by the Oxford team, of which, as is generally known, Sir Robert Robinson is the senior chemist. At about the same time—and it is presumed independently—synthesis was also achieved by the Merck organization in New Jersey. The yield was, however, only about one-tenth of 1%; and in addition the synthesis was not of such a kind as to be chemically informative. No attempt was therefore made by the Oxford workers to prepare synthetic penicillin in chemically pure form by this method. Instead, later efforts have been directed, so far without success, towards the development of a further synthesis of greater practical utility. Subsequently a second American team, working in the Department of Biochemistry of Cornell University Medical College, applied the original method of synthesis to produce a small supply of chemically pure penicillin II. The Oxford synthesis was of penicillin I. But since the method, within its obvious limitations as to yield, is generally applicable to all the penicillins, the distinction is of no significance. The present paper, which is of a preliminary character, is the work of the Cornell team—Du Vigneau, Carpenter, Holley, Livermore, and Rachele. It is published in *Science* of Nov. 8, the journal of the American Association for the Advancement of Science, with due credit to the earlier work both at Oxford and in the Merck laboratories. Authority for publication in this form was given by the joint Anglo-American committee which is responsible for the release of information on the work which has been carried out for the Committee on Medical Research of O.S.R.D. in the United States and the Medical Research Council in Great Britain. The result takes us little if any further as regards knowledge of penicillin, but among the general public in the United States it has given rise to the erroneous impression that the first synthesis of penicillin was a purely Cornell achievement.

## REITER'S DISEASE

The symptom complex known as Reiter's disease—conjunctivitis, arthritis, and urethritis—appears to be a definite disease entity, though reference to standard textbooks provides little or no information on the subject. The condition was first described by Reiter[1]; and soon afterwards Fiessinger[2] in France and Macfie[3] in Africa recorded some cases. Most of the earlier cases occurred in France, Germany, and Scandinavia. Little more was heard of the condition for some years, but recently other cases have been reported, including ten from the Pacific area and six

1 *Dtsch. med. Wschr.*, 1916, **42**, 1535.
2 *Bull. Mém. Soc. méd. Hôp.*, Paris, 1916, **40**, 2030.
3 *Parasitology*, 1917, **9**, 274.

from Boston; and Vallee,[4] in a review of the literature, refers to 151, while Touraine and Ruel[5] put the number at about 300. The latter authors call it "pseudo-gonococcal enteritis," whereas Sargent[6] proposes the term "idiopathic blennorrheal arthritis."

Almost all the described cases are in males (usually young); there is no relation to sexual intercourse. Some French observers consider that the condition is associated with dysentery or other intestinal infections. In the light of recent war experience Paul Wood,[7] Marsh,[8] Herson,[9] Kay,[10] and Manson-Bahr[11] all correlate the disease closely with bacillary dysentery, but Jackson[12] shows that no identification with these bacilli has yet been made and that his two cases developed in an area where bacillary dysentery was unknown. The conjunctivitis is purulent or mucopurulent, and often bilateral; there is some photophobia and lacrimation; and there may be scleritis, iritis, and keratitis as well. The urethritis is characterized by a purulent discharge, but frequency and dysuria are not as marked as would be expected, though haematuria may occur. The arthritis affects mainly the larger joints, flitting from one to another, and imitating acute rheumatism; hydrarthrosis is common. In addition there is usually a low-grade fever. Skin rashes often appear; they start as vesicles which rupture and form shallow ulcers, and these heal leaving hyperkeratotic scars. Harkness[13] records three cases which resembled keratodermia blenorrhagica. Generalized lymphadenitis is a frequent accompaniment; there is a moderate polymorphonuclear leucocytosis, and the erythrocyte sedimentation rate is slightly increased. All three typical signs are not always present, and consequently the differential diagnosis may be from rheumatic fever, gout, acute conjunctivitis, prostatitis, balanitis, keratitis, iritis, non-specific urethritis, and arthritis.

The causal organism was thought by Reiter to be a spirochaete, but this has not been confirmed. Harkness claims to have demonstrated inclusion bodies, but modern opinion inclines to the view that a virus is the probable causal agent. Pathological examination of the urethral and conjunctival discharge and of fluid aspirated from the affected joints has failed to incriminate any particular organism. The gonococcus has never been found. Blood cultures are uniformly negative, as are gonococcal complement-fixation tests, serum tests for syphilis, and agglutination tests against dysentery and typhoid bacilli. Treatment is mainly symptomatic, though some success has been claimed with sulphonamides and arsenicals, as well as with protein-fever therapy—it seems not unlikely that artificially induced pyrexia by means of a Kettering hypertherm or similar appliance may be beneficial (King[14] *et al.*). It may be noted that two of Fieldsend's[15] cases diagnosed as abacterial pyuria had arthritis. Were they cases of Reiter's disease? If so it is of interest to observe the favourable response of the urethritis to neoarsphenamine. The disease is self-limiting, though it is apt to drag on for several months, and relapses are not uncommon.

Cases recently reported in this *Journal* by Wrigley[16] and Jackson[17] are of interest as showing that the disease is probably not nearly so rare as has been supposed. The combination of urethritis with arthritis has led to many cases falling into the hands of the urologist or the venereologist. This combination is so common in gonorrhoea, often with conjunctivitis as well, that the practitioner can hardly be blamed if he makes a provisional diagnosis of gonococcal, or at any rate of infective, arthritis, though he will be saved from the former error if he has the benefit of, and faith in, adequate pathological facilities such as culture examinations and complement-fixation tests. Denfield,[18] as a result of observation of its association with gonorrhoea in West Africans, hints at an allergic origin of the syndrome, as it requires more than one attack of gonorrhoea to provoke it, and, when provoked, subsequent attacks of the acute urethritis successively intensify the Reiter's disease.

4 *Arch. intern. Med.*, 1946, **77**, 295.
5 *Ann. Derm. Syph.*, Paris, 1946, **2**, 61.
6 *J. Urol.*, 1945, **54**, 556.
7 *British Medical Journal*, 1946, **2**, 309.
8 Ibid., 1946, **2**, 276.
9 Ibid., 1946, **2**, 275.
10 Ibid., 1946, **2**, 309.
11 *Bull. War Med.*, 1944, **4**, 653.
12 *British Medical Journal*, 1946, **2**, 403.
13 *Brit. J. vener. Dis.*, 1945, **21**, 93.
14 Ibid., 1946, **22**, 1.
15 *British Medical Journal*, 1946, **2**, 493.
16 Ibid., 1946, **2**, 199.
17 Ibid., 1946, **2**, 197.

## WORLD LIST OF SCIENTIFIC PERIODICALS

Active preparations are being made for the issue of a third edition of the *World List of Scientific Periodicals*. The last edition of this invaluable scientific reference work, issued in 1934 and covering the years 1900–33, is now out of print though still in constant demand. It contains upwards of 33,000 titles of journals and includes the holdings of some 180 libraries in Great Britain and Ireland. The new edition, which is designed to include all the scientific and technical periodicals that appeared during the period 1900–47 as well as the holdings of additional libraries, will therefore be considerably larger. Librarians are being asked to co-operate as before by sending particulars of all those journals on their shelves that do not appear in the second edition, or are shown there as having no location in this country, to: The Secretary, World List of Scientific Periodicals, c/o The Zoological Society of London, Regent's Park, London, N.W.8. Further information may be obtained from this office.

Sir Arthur MacNalty will give the FitzPatrick Lectures before the Royal College of Physicians of London on Dec. 10 and 12 at 5 p.m. His subject is the History of State Medicine in England: Lecture 1, "From the Accession of Queen Victoria to the General Health Board"; Lecture 2, "The Medical Department of the Privy Council."

The President and Council of the Royal Society have awarded the Copley Medal to Prof. E. D. Adrian, O.M., M.D., for his researches on the fundamental nature of nervous activity, and more recently on the localization of certain nervous functions.

18 *British Medical Journal*, 1946, **2**, 555.

Col. Malcolm Stoddard-Scott, M.D., Conservative M.P. for Pudsey and Otley, has presented to the Minister of Health a memorandum urging that Bradford hospitals should be classed as teaching hospitals under the National Health Service Act. The memorandum was prepared by a committee of local authorities in Bradford after considering in detail the requirements for a medical faculty in that city. In the committee's view Bradford could provide accommodation, teachers, and clinical material for a medical school, and could from October, 1947, train 50 undergraduates a year. In a letter to the Minister Col. Stoddard-Scott informs him that the Bradford Technical College already trains undergraduates for the first part of the London M.B., and is recognized by London University for that purpose. If a medical school is established in Bradford it would be prepared to train undergraduates for the final M.B. of London and Leeds Universities, and would also admit students wishing to take the English and the Scottish conjoint examinations and those for the licence of the Society of Apothecaries. Medical and surgical work under the scheme would be carried out in the Bradford Royal Infirmary, St. Luke's Municipal Hospital, the Royal Eye and Ear Hospital, the Children's Hospital, the City Fever Hospital, the Bierley and Grassington Sanatoria, and the Rawdon Rehabilitation Centre.

# ADAPTATION OF E.M.S. HUTS FOR CHILDREN'S WARDS

BY

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In the report of the British Paediatric Association's *ad hoc* committee on cross-infection in children's wards, published in the *B.M.J.* (May 4, 1946, p. 673), sections 6 and 7 deal with the subdivision of wards and other desiderata. With the recommendations of this report in mind, we prepared a plan to show how a typical E.M.S. hutted ward may be modified at reasonable cost and with minimal structural alterations to accommodate infants and children in surroundings where the chances of cross-infection are lessened and other desiderata are provided.

Just after the preparation of our plan, the Ministry of Health published a series of plans, including one for a children's ward, prepared by Dr. T. S. McIntosh and Mr. H. R. Coales, on the adaptation of E.M.S. huts for peacetime hospital purposes (Supplement to the *Monthly Bulletin of the Ministry of Health*, February, 1946). Our plan is not intended to rival or better theirs; indeed, Dr. McIntosh and Mr. Coales point out that it is all to the good that different methods of adaptation should be explored.

Figs. 1 and 1a show the proposed adaptation and the existing E.M.S. hut in Warwickshire, respectively. Figs. 2 and 2a are reproduced from the Supplement to the *Monthly Bulletin*, by permission of H.M. Stationery Office, for comparison.

E.M.S. huts vary, and the type chosen by the Ministry is admittedly the most difficult to adapt architecturally, with its flat roof and central supporting pillars. It differs structurally from those existing in Warwickshire County Council hospitals in the following details:

| *Fig. 1a (Warwick)* | *Fig. 2a (Ministry)* |
|---|---|
| Pitched roof 35° | Flat roof with central columns in ward |
| Floor to eaves in ward, 10 ft. (3·05 m.) | |
| Ceiling, 12 ft. 8 in. (3·86 m.) | Ceiling, 10 ft. 1 in. (3·07 m.) |
| Four pairs of doors in each long wall | Two pairs of doors in each long wall |
| *Arrangement of Ancillary Rooms* | |
| Overall length, 36 ft. 4 in. (11·07 m.) | Overall length, 40 ft. (12·2 m.) |
| Ceiling, 9 ft. 8 in. (2·95 m.) | Ceiling, 8 ft. 1 in. (2·46 m.) |
| Corridor, 5 ft. wide (1·52 m.) | Corridor, 6 ft. wide (1·83 m.) |
| Sluice, 9 ft. 1 in. (2·77 m.) by 8 ft. (2·44 m.), adjacent to W.C.s. | Sluice, 9 ft. 7 in. (2·91 m.) by 8 ft. 7 in. (2·62 m.), adjacent to ward |
| Kitchen adjoining ward, with observation window | Servery near entrance |
| No store-room | Store-room, 8 ft. 7½ in. (2·63 m.) by 7 ft. (2·13 m.) |
| Small heating chamber for domestic hot water, towel rails, and radiators | No heating chamber. Hot water presumably from central service |

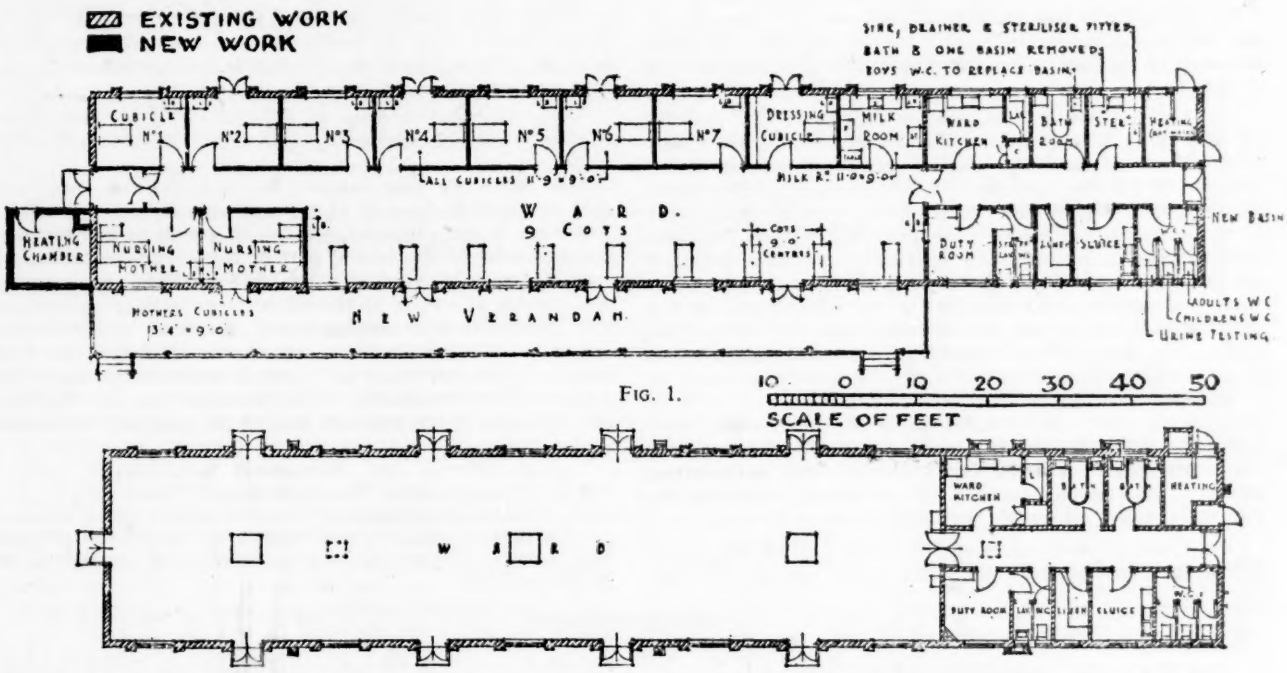


FIG. 1.

FIG. 1A.

Plan showing typical 32-bedded hutment adapted to provide a children's ward with protection against cross-infection. FIG. 1.—Plan after alteration; accommodating 7 cots in separate cubicles, 9 cots in open ward, 2 cubicles for nursing mothers, 1 cubicle for dressings. Cubicles to have plug point and lavatory basins in each. FIG. 1A.—Plan before alteration—32 beds.

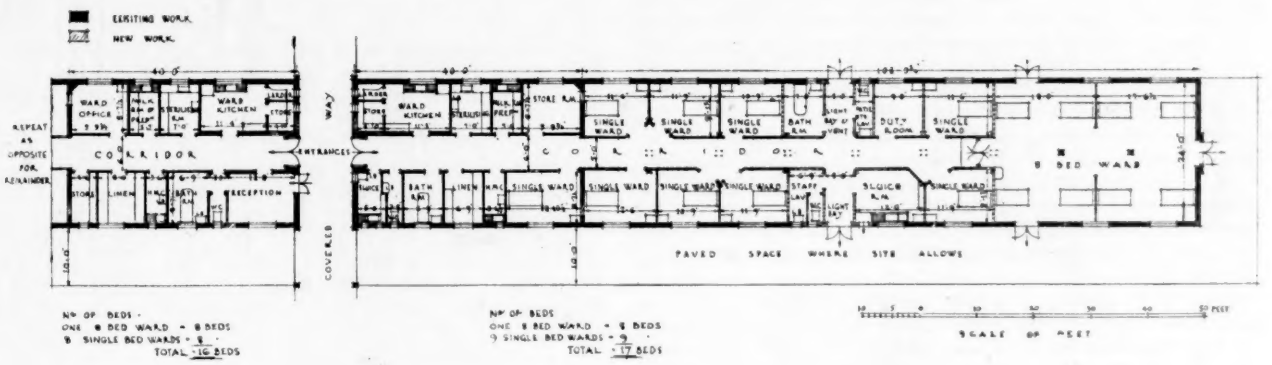


FIG. 2.

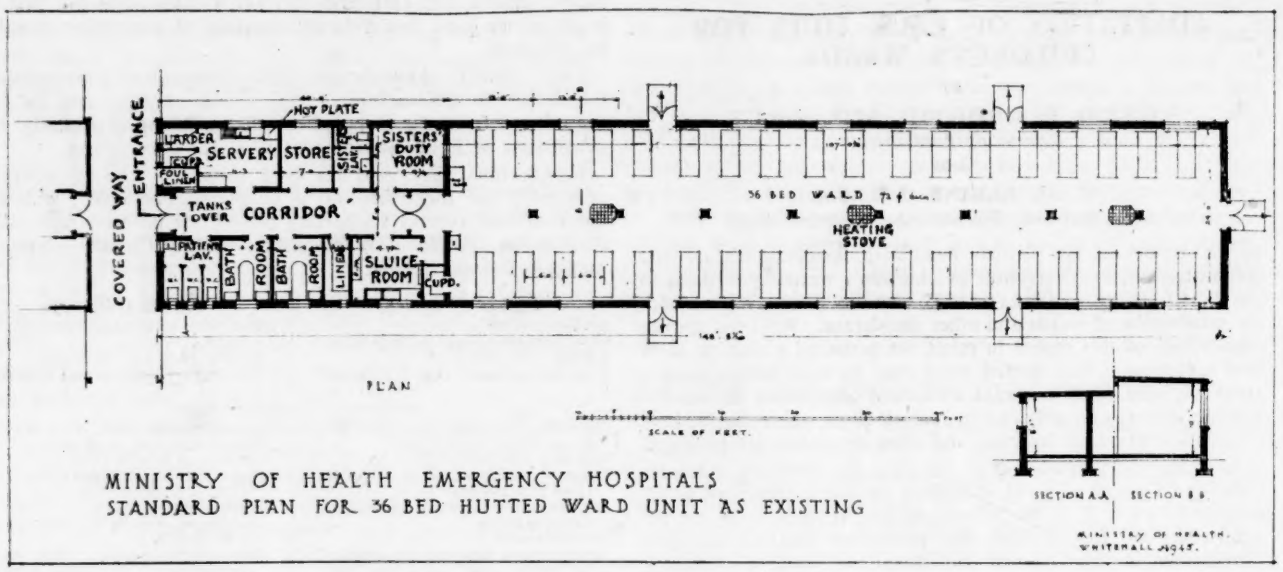


FIG. 2A.

The total length and breadth of each ward are the same—viz., 108 ft. (33 m.) by 24 ft. (7.3 m.), so that the differences are really of a minor nature and chiefly limited to the ancillary rooms.

The ward as existing has accommodation for 32 patients. By subdividing it into cubicles (Fig. 1) this number is reduced to 18. Seven of the cubicles are single, which provides a percentage for isolation considerably higher than the 25% minimum recommended by the subcommittee. The 9-bedded open ward allows of a friendly communal atmosphere for older children, who do not need the strict isolation that is necessary for young infants. It should be a rule that no infant under 1 year of age is to be admitted to an open ward. It will be seen that there are two cubicles provided for nursing mothers and their infants. When there are no breast-fed babies in the ward these cubicles could of course be used as single cubicles for children, or two infants could be nursed in each, bringing the total beds available up to 20. (The word "cot" in the plan refers equally to a child's bed.) The existing heating arrangements consist of three centrally placed coke-burning stoves. These are not suitable for a children's ward, and we have substituted an outside heating chamber.

One of the subcommittee's special points was the desirability of having a separate room in which to do surgical dressings, lumbar punctures, aspirations, etc., and this is provided. There is also a small room for testing urines. The milk-room, which is 11 ft. (3.35 m.) by 9 ft. (2.74 m.), is more adequate in size than the one proposed by the Ministry, which is only 8 ft. 7½ in. (2.63 m.) by 5 ft. (1.52 m.). In our plan, the ward and all the cubicle doors can be under direct supervision from the duty room.

The Ministry's plan allows for a store-room 9 ft. 9 in. (2.97 m.) by 8 ft. 7½ in. (2.63 m.), a housemaid's closet, and an additional sluice. This arrangement of a sluicing compartment and lavatories in the central part of the ward is advantageous from the point of view of access, but we wished to undertake a minimum of structural alteration in our plan, in which cost was also taken into consideration. We think one bathroom would be sufficient, but if necessary the end bed in the open ward might be sacrificed and a small bathroom, lavatory, and sluice included for the use of the nursing mothers. The other modifications in the ancillary part of the ward are as outlined in the plan.

**Summary**

A plan is suggested for the adaptation of a typical E.M.S. hutted ward for the accommodation of 7 babies in single cubicles, 9 children in an open ward, and 2 nursing mothers with their infants, together with a room for dressings, a milk kitchen, and the other usual ancillary offices.

## SOCIETY OF APOTHECARIES AWARD TO PENICILLIN DISCOVERERS

At a special meeting of the court of the Society of Apothecaries of London on Nov. 28 Sir Alexander Fleming and Sir Howard Florey were presented with the Society's gold medals in therapeutics in recognition of their discoveries in penicillin. The presentation was made by Dr. C. Thackray Parsons, the Master, in the presence of a large number of freemen and of guests, who included Sir Alfred Webb-Johnson, President of the Royal College of Surgeons, and Sir Hugh Lett, President of the British Medical Association. The Master referred with pride to the addition of these names to those of Dixon, Gowland Hopkins, Dale, Banting, and others on the Society's roll of medallists. "In the nurseries of the future the contaminated Petri plate of Fleming will probably displace the legend of Newton and the apple, and as future generations eat their prophylactic breakfast of mixed moulds they will pray for the good estate of Fleming and Florey."

Prof. E. C. Dodds, in a brief oration, compared the present occasion to the gathering at the Sorbonne in 1892, when Pasteur on his seventieth birthday was acclaimed by the President of the French Republic and a distinguished company which included Lister. In the work of Fleming and Florey they saw one of the last acts in the drama which opened with the work of Pasteur. The veil of mystery which for centuries had covered the processes of infection had been rent, and an uncertain empiricism had given way to scientific principle. Never before in the history of the world had it been possible to honour two men who had been personally responsible through their labours for the fact that literally millions of people to-day were alive who would otherwise be in their graves, and, unlike many brilliant discoveries of science, not even the most malignant mind could suggest that this discovery could be applied in an offensive or destructive manner.

Sir Alexander Fleming, in receiving the medal, said that it had been his good fortune—he emphasized the word "fortune"—to be in at the beginning of a movement which had done something for medicine and surgery. He contrasted the conditions obtaining in the first world war with those obtaining in the second from the particular point of view of fracture of the femur. In 1918 he was in charge of a hospital for cases of fractured femur, and it was a grim experience, very different from that which attended these cases during the recent war. Not all the difference, of course, was due to penicillin, but it helped. He paid a warm tribute to his co-recipient.

Sir Howard Florey also spoke of his own good fortune in being associated with Sir Alexander Fleming in a work which had proved of value in medicine. The experience had been for him particularly exciting, because it had given him the opportunity of travelling all over the world and of meeting thousands of people. Coming as he did from a young country (Australia), he perhaps more than those in England appreciated the antiquity of the hall in which they had met and the general setting of the ceremony. He added that they were only just beginning to realize the extraordinary series of fortunes with which this work on penicillin had been favoured. There were 100,000 species of moulds such as those that rotted timber or grew in the fields; there were 15,000 species of *Ascomycetes* to which penicillium belonged, and there were several hundreds of species of penicillia. Many of these produced chemical substances and, almost without exception, they were extremely poisonous. Yet penicillin was the first one to be examined in any detail, whereas it might well have been one of the other thousands of organisms, and they might have endeavoured to extract the active substance and, realizing that it was extremely poisonous, have abandoned the investigation.

Occasion was also taken to make a presentation to Mr. W. T. Withers, who is retiring from the position of bedel of the Society after fifty-nine years' service.

## ROYAL COLLEGE OF SURGEONS AND THE ACT

### SPECIAL MEETING OF FELLOWS

A special meeting was held at the Royal College of Surgeons of England on Nov. 29 following upon a requisition made by a number of Fellows and Members at the Annual Meeting of the College earlier in the month. The purpose was to consider the position which has arisen consequent upon the passing of the National Health Service Act. Sir Alfred Webb-Johnson presided and there was a very large attendance.

#### The Council's Corporate "Yes"

The President said that in the College they had always done their best to approach this question non-politically. They regarded the freedom of the profession, not as a vested interest, but as guarding one of the fundamental rights of a citizen in a free country. They had contended that the Negotiating Committee should be supported because it was representative of the whole profession; they had always resisted attempts to undermine its authority, and they had desired to support their general practitioner colleagues. Four important points affecting general practice remained in the Act, notwithstanding the endeavour to get them removed: prohibition of the sale and purchase of practices; restriction on the individual practitioner as to where he should practise; the setting up of a tribunal (with final appeal only to the Minister) which had power to decide that a practitioner should no longer remain in the Service; and remuneration by basic salary (this last not in the Act but in the White Paper and in the intention of the Minister).

Personally he confessed that he did not think any of these items sufficient ground for refusing to discuss the implementation of the Act and the planning of the Service. The most important was the salary element in the remuneration of general practitioners, which might undermine the doctor–patient relationship. On principle he thought it undesirable, but he recognized that a considerable number of young men would welcome such an arrangement. In hospital practice the most serious thing was that the Act created a monopoly of hospital surgery. That might have serious effects, but he did not know that they could refuse to discuss the Act with the Minister because he was taking over the hospitals. By negotiation it might be possible to induce him to frame regulations whereby the patient would be left with as much freedom as he had at present. It was undesirable that the Minister should be empowered by regulations to control the fee charged for all patients admitted to the paying blocks of hospitals; it was said that the ceiling would be high, but that was not the point. The point was that in some of the accommodation in the private wings of hospitals there should be complete freedom of relationship between doctor and patient, though he agreed that in some portion of such accommodation there should be some control so that people of moderate means might be able to be accommodated privately. What might be obtainable by negotiation was the preservation of independent practice. That was an important thing for a free profession.

"I have fought for all these things," Sir Alfred Webb-Johnson concluded, "at the stage when the law was in the making. Considerable concessions have been obtained during the passage of the Bill; I believe considerable concessions may be obtained in the form of regulations. The Council has to answer in a corporate capacity the question whether it desires the Negotiating Committee to enter into discussion on the framing of such regulations. As a corporate body the Council has answered 'Yes.' As individuals it is for each of us to make up his own mind."

#### Runnymede or Munich?

Mr. Lawrence Abel opened for the opposition. He quoted resolutions of the Council of the College, especially those of May 8 last, expressing opposition to certain proposals which were then in the Bill and now remained in the Act. He also quoted from the reported speeches of the President of the College, warmly supporting the case of the general practitioners and protesting against State monopoly and other dangers. It was said that the Act was only the bones of the scheme and the regulations would clothe this skeleton with flesh. But the "bones" were ill conceived, they were worm-eaten and decalcified, and the more flesh that was put on a rachitic skeleton the greater would be the deformity. He asked the Council of the College, "Are you going to let your Fellows down?" If they were convinced that their principles remained sound they would answer "No" in this plebiscite. Was this to be their Runnymede or their Munich?

Mr. W. Etherington-Wilson said that he had come up from the West Country with the expectation of his colleagues that he would return with the assurance that at all costs the Royal College of Surgeons was going to stand rock-like for the principles which the profession had established.

#### A New Act of Uniformity

Mr. Reginald T. Payne said that the question now was whether the profession was to negotiate on regulations. Regulations would not alter the principles of the Act, but only its details. The implications of this Act were far wider than its application to the medical profession: they opened up important constitutional and legal considerations. Was a Government department to be entrusted with the powers which this Act conferred on the Minister? Further, was a monopoly of medicine justified in a democracy? If they answered these questions as members of a liberal profession their duty and responsibility to the community would take them far away from merely personal or professional answers. The catchwords of the age were "organization" and "efficiency," but these could be gained at too great a sacrifice of freedom. In Italy under Fascism the trains ran much more punctually, but intellectual and political liberty disappeared.

Mr. Payne entered upon a lengthy discussion of constitutional aspects. All parliamentary business was now extremely hurried, which meant lessened parliamentary control and a greater dependence on regulation. The judiciary was short-circuited. This Act was an outstanding example of delegated legislation. Quasi-judicial bodies were gradually being developed in this country—bodies which often sat *in camera*, and from whose findings there was no appeal. Under this new Act there could be no appeal to the courts by any dismissed doctor. It also created a State monopoly of medicine. It was an Act of Uniformity for the better discipline of doctors and patients. The consultant would be "directed," it would be a case of "join the Service or be liquidated." The student would be "grant-aided, State-conditioned, and rendered servile, mobile, and docile." What about the Royal College? In ten years' time half the Council would be civil servants in all but name and the other half would be Government pensioners. If this Act was operated it would be necessary to restart independent institutions in the interests of the public and of medicine. Fundamental democratic rights would have to be re-established and reasserted. In a democracy there must be a right to dissent.

His own sympathies for many years had been with the Labour Party, but he was terrified by the position into which

they were now forcing the community. The crisis was comparable with that of the seventeenth century on the issue of liberty versus the tyranny of central power. Then it was a question of kingship and religion, now it was a question of the executive and political and social theory. He begged them to stand for their essential freedom and not to become Government pensioners with their minds in cold storage. The power which the central organization had in this Act meant coercion and regimentation. The analogy with 1912 was false. We had not then a dictator-ridden world. Of the National Health Service Act he could only use colloquial language and say that it "stinks of dictatorship." It was a whip in the hands of the executive. "You can negotiate, if you are going to negotiate, on how the whip should be used."

### A Resolution Not Put

Dr. N. E. Waterfield proposed the following resolution:

> That this meeting of Fellows regrets the decision of the Council to recommend members of the College to agree to enter into negotiation with the Minister on the regulations to be made in connexion with the new National Health Service Act, as the decision runs counter to the feeling of the meeting of the Fellows here present.

This was seconded by Mr. Lawrence Abel.

The President said that he was unable to accept the resolution; it stated what was not a fact. The Council had made no recommendation to the Fellows and Members. He had taken the trouble to explain very carefully in his opening remarks that it was for each man to decide for himself.

Dr. Waterfield: I thought you said that the Council had come to a decision in its corporate capacity.

The President: I said that the Council had instructed me what to reply as a College. This meeting has been called at short notice for the purpose of exchanging views. Up to now certain people have monopolized the platform. Is there any contrary view?

Major J. S. Horn said that he thought they should answer "Yes" in the plebiscite. They had been urged to say "No" because it was stated that certain fundamental points of principle were at stake. There were certain points in the Act which they all agreed were bad, but others which they all agreed were good, and it seemed to him of first importance not to confuse points of principle with expediency. He thought that the scheme, which was brought forward by a Government recently returned to power at a general election, should be accepted and the best possible job made of it.

Mr. C. E. Beare said that it was a sad day for him to find himself not in agreement with Sir Alfred Webb-Johnson, for he admired so much the way he had worked for the profession. But the British Medical Association, which represented over 50,000 members of the profession, had instructed its representatives to take a firm stand on certain principles, and those principles had been established by votes of between two and three hundred to an insignificant minority, if not unanimously. Having affirmed those principles, how could they possibly negotiate merely on regulations and terms of service? The report of the Negotiating Committee declared that the independence of medicine was at stake. On a recent Sunday he visited between 20 and 25 doctors in his locality and there was not one "Yes" among them, and at a meeting of 80 practitioners at Reigate there were only eleven affirmatives. The majority included a number of young men who said: "We thought we had been fighting for freedom, and we come back to find dictatorship imposed upon us."

Mr. Dickson Wright said that he was perturbed at the prospect of hospitals being a public monopoly. Free choice of hospital was just as important as free choice of general practitioner. There would be no medical committee in Government hospitals. Consultants would be directed from hospital to hospital in the most unpleasant way. Direction was even more unpleasant for the established consultant than for the young general practitioner, for it was hard to settle down in a new place when one was fifty. A State monopoly of medical treatment would lead to loss of morale in the profession. Doctors were not going to strike, but they were at liberty to say, "We are not going to work for you." When the Government had overstepped its mark there was nothing wrong in one section of the community making a sacrifice if necessary and putting its foot down and saying, "We are not going to do this, not because we are afraid of having less money, but because we think it is a bad thing. We want free choice of hospitals." He felt strongly that this consultant body should have been recommended to say "No" in the plebiscite.

Mr. Sangster Simmonds said that the result of this Act was not going to depend on the regulations with which they were so much concerned, but on the way in which the medical profession did its work. The success of voluntary hospitals had been achieved because the physicians and surgeons on their staffs had done their work well. The success of this Act would depend on individuals and how they worked, not on Regulations from Whitehall. The old Insurance Act was a piece of legislation which the profession did not help to negotiate but which was forced upon them, yet the profession had made a success of it.

### Concurrence with the Main Body of the Profession

Mr. A. J. Gardham said that he found it difficult to say in the same breath that he disapproved of the principles of the Act and that he wished to participate in the framing of its Regulations. He desired to move a resolution on one matter on which he felt strongly:

> That with regard to the National Health Service Act the Royal College of Surgeons of England shall take no action which is not in accord with the wishes of the main body of the profession.

Such a resolution might save the College from a disastrous decision.

The President: What do you mean by "the main body of the profession"?

Mr. Gardham: That is a matter we should have to ask the Council to decide.

The President: I was very anxious to avoid putting any definite resolution to this meeting, because this is a meeting called at short notice for the expression of views. Any formal resolution should have been circulated with the notice.

Mr. Gardham said that he had put forward the resolution, not with a view to instructing the Council, but as a means of assuring the profession at large that the surgeons were with them and not against them. (Loud applause.)

The President: Will it satisfy those who have brought forward this resolution and the meeting generally if a notice is sent to the Press stating that it was generally agreed that the College should act in conformity with the general feelings of the profession in regard to the question of negotiations on the regulations of the Act? (General murmurs of assent.) The President added that the Council had told the Negotiating Committee what the College recommended concerning negotiation, but if other members of the Committee did not concur and the general feeling was in a different direction the recommendation of the Council would not carry. Why should he be put in this quandary regarding what the earlier resolution called the "decision of the Council"? It was not quite fair to him.

Dr. Waterfield said that the Council, apparently, was not desirous of knowing the feeling of the Fellows generally. He asked that his resolution should be put.

The President said that the decision of the Council as representing a corporate body was not binding upon any individual. The Council had thought it to be its duty to recommend agreement to enter into negotiations. He did not think it fair, on the strength of that, to be asked to put a resolution to the meeting regretting the action of the Council. Members might not know how difficult and distressing the position of leaders of the profession might be.

Dr. Waterfield said that he was prepared to withdraw his resolution.

The President: Thank you very much. I appreciate your anxiety that the College should take a firm stand. I will convey to the Council the general feeling of this meeting and will include in a communication to the Press a statement that this College will stand loyally by the majority of the profession, whatever their decision may be.

In reply to Mr. T. A. Green, the President said that a considerable majority of the Council had voted in favour of negotiation. What reasons moved them he could not say. It might

have been his persuasive eloquence, though he did not unduly try to influence them. He thought they felt that they were going to get very poor support from the public if at this stage they refused to negotiate, whatever might happen at a later stage. It must be admitted that they had not had a very good Press up to now. He himself held the view strongly that at this stage it was their duty to negotiate.

The meeting then terminated. It was attended by 150 Fellows, and although no vote was taken the volume of applause suggested that there was a large majority against negotiation.

## PRIORITY SUPPLIES OF MILK TO INVALIDS

On Oct. 29 the Minister of Food made a statement on milk certification. He implied that there had been laxity by doctors in issuing their certificates and announced that all certificates issued before Nov. 3 must be renewed on or after the 30th of that month unless their time expired before that date. It will be recalled that the matter was discussed at the November Council Meeting and a strong protest issued.

The Minister's announcement was made in the Press, in the *British Medical Journal* (Nov. 2, p. 661), and over the wireless, but this method of notification resulted in a certain amount of confusion. Doctors had not been notified personally, and consequently only those who saw or heard these announcements were aware that certificates must be reissued. The result has been that doctors have been annoyed by frequent demands from their patients for renewed certificates, and patients have been unable to obtain their priority needs of milk.

Practitioners are reminded that patients are unable to obtain their priority supplies of milk unless they submit a certificate issued after Nov. 3.

# Reports of Societies

## TREATMENT OF ACUTE PERITONITIS

At a meeting of the Section of Surgery of the Royal Society of Medicine on Nov. 6, with Mr. E. F. FINCH in the chair, Prof. JOHN MORLEY said that he would confine himself largely to the diffuse or general infection of the peritoneum rather than deal with the localized abscess. Surgical opinion had passed through various stages since Lister laid the abdomen open to surgery. When surgeons at last put aside their unreasoning dread of the peritoneum their reaction was to treat it with far too little respect for its delicate defence mechanism. At one time there was a great belief in the drainage of the peritoneum, and the abdomen after an operation would be left bristling with tubes. A great step forward from the vigorous and ill-advised flushing was made when gentle sponging of the peritoneum with swabs wrung out of normal saline took its place, later to be replaced by suction. The greatest advance in treatment was the realization of the important part played by dehydration in peritonitis, the loss of water and sodium chloride from the blood, and the practice of replacing this fluid by normal saline given at first by the rectum and subcutaneously and later by the intravenous route. A further step forward came with the introduction of the Ryle tube, and the crowning mercy was chemotherapy. As the vast majority of the cases of peritonitis were secondary to perforations of the alimentary tract, he would put first among the principles of treatment the closure of the ulcer or removal of the appendix. The operation itself, necessary though it was, did inevitably add somewhat to the risk of paralytic ileus, which was in its essence a defence mechanism. He preferred the term "inhibition ileus" as emphasizing the initial state when treatment could do some good; later, when the gut was distended with gas and fluid and oedematous or inflammatory changes had taken place and there was a failing circulation, the wall of the gut became truly paralysed and a stage was reached when the paralysis was irreversible. The fundamental difference between inhibitory or paralytic ileus and mechanical ileus must be emphasized. Peritonitis, of course, often led to mechanical ileus by causing fibrous adhesions which resulted in kinking, torsion, or compression of the bowel. Operation should be carried out with the least possible trauma, and that was the main reason why, in addition to spinal anaesthesia, an adequate incision and suction should be used rather than sponging to cleanse the peritoneum of infected fluid.

### Should the Peritoneum be Drained?

Should the peritoneum be drained? The answer in perforated peptic ulcer was emphatically "No." He had not drained a perforated peptic ulcer, except in an occasional late case with subphrenic abscess, for twenty years; drainage was unnecessary and was likely to give rise to dangerous adhesions. In peritonitis from a gangrenous appendix he seldom drained unless an abscess cavity was present which was prone to bleed, but always drained the abdominal wall if it was heavily contaminated. In general, drainage of the peritoneum did very little good, though when in doubt there was no great harm in draining for a day or two. On the subject of chemotherapy there was still no unanimity as to which was the best drug to use or the best manner of its application. It was bad practice to apply masses of sulphonamide powder within the peritoneal cavity; a much sounder method was to introduce it in suspension in normal saline. It was a matter for discussion whether intraperitoneal applications of the sulphonamides should be supplemented by sulphonamides given by the intravenous route or by penicillin.

Within recent months two vigorous tugs had been made at the pillars of the house of surgical orthodoxy—namely, Spalding's attack on the time-honoured Fowler position and Hermon Taylor's advocacy of the non-operative treatment of perforated peptic ulcer. The belief that Fowler's was the best position to protect the patient from subphrenic abscess formation did not emerge unscathed from Spalding's attack. Without subscribing to all the arguments about the hydraulics of the peritoneal cavity the contention concerning the limitation of breathing when the patient was propped up in the Fowler position was impressive and Prof. Morley felt that Spalding had made out a good case against it. Hermon Taylor's plea for the expectant treatment of perforated peptic ulcer was less convincing. In a patient who was a bad operative risk owing to old age or chronic bronchitis it was preferable to try expectant treatment, but in the average risk, if one got the perforation early—within the first six hours—he would not advise it. It was wrong to regard the present operative mortality as serious. In the last 24 cases of perforation on which he himself had operated there was only one death (of a man who had perforated five days before and had a subphrenic abscess), and in his unit in Manchester Royal Infirmary during the last five years in 100 cases of acute perforation there had been only 8 deaths, all of them in patients who were either bad risks by reason of bronchitis and emphysema or in whom the perforation had taken place more than twenty-four hours before.

### Protein Balance

Mr. C. G. ROB said that recovery from established acute general peritonitis, while depending to some extent upon the skill of the operating surgeon, was governed to a far greater degree by the pre- and post-operative care which the patient received, and one factor in ward care was protein balance. From the investigations on protein metabolism during the late war some surprising facts about the easily estimated plasma proteins came to light. For example, the patient with chronic long-standing wound sepsis usually had a normal plasma protein level although considerable protein loss had occurred. In burns or acute peritonitis the plasma protein level might fall before the tissue protein could be mobilized to replace the loss. Patients with established acute general peritonitis suffered from reduction of body proteins which occurred in four principal ways: (1) exudate from the surface of the peritoneum; (2) into the lumen of the distended intestine when paralytic ileus had occurred; (3) into the subserous and serous layers of the peritoneum, and (4) owing to associated reduction of protein digestion. Mr. Rob entered upon a description of the mechanism involved, leading up to a fact of great clinical importance, namely, the need of giving a

plasma transfusion to every patient whose peritoneal infection was severe enough to require an intravenous infusion, thereby maintaining the plasma protein at normal level. Not only would such a procedure prevent the onset of peripheral circulatory failure, but if given in sufficient quantity it might even correct established peripheral circulatory failure in an apparently moribund patient. During the past three years he had treated 31 patients who had established general peritonitis and had placed them on a post-operative regime which included plasma transfusion. In 25 of those who received the plasma transfusion before there was peripheral failure no sign of such failure developed, and all made a satisfactory recovery. The other six did not receive a plasma transfusion until after peripheral circulatory failure had developed. They were moribund, with a very rapid and thready pulse and a subnormal temperature; but in spite of this three of them recovered, due no doubt to the very large amount of plasma they received. Every patient whose peritonitis was severe enough for an intravenous infusion to be necessary should receive plasma as a prophylactic measure against the peripheral circulatory failure to which such patients so often succumbed.

### General Discussion

Mr. VAUGHAN HUDSON spoke of the value of penicillin as an auxiliary in the treatment of peritonitis or as a preventive of complications. There was a definite place, as war experience had shown, for parenteral penicillin in all injuries from without. The failure of the sulphonamides to prevent the post-operative complications of pneumonia after collapse of the lung and infections in the renal tract was disappointing; but the control of these complications by parenteral penicillin was encouraging. Mr. NICHOLSON criticized Fowler's position. In a unit with which he had been connected the practice was to have the patient flat on the back, and in that position the subject did as well as in Fowler's position. Many patients did not like Fowler's position, and more harm than good was done by compelling them to be in a position in which they were uncomfortable. Prof. IAN AIRD spoke of the difficulty of estimating the value of the sulphonamides and penicillin in a condition such as peritonitis owing to the absence of a control series. An attempt at a control series was made in the children's hospital in Edinburgh, but the figures obtained were not significant.

Sir HENEAGE OGILVIE said that towards the end of the war nearly every surgeon dealing with abdominal injuries adopted the principle of replacing lost protein by intravenous plasma, but the methods used were very haphazard. It was very interesting to find it put on an experimental basis by Mr. Rob. In peritonitis they were perhaps too apt to be concerned with the bacterial side. Certainly peritonitis was an abscess in the largest cavity of the body, but surely it was a cavity which could deal with infection better than any other. He agreed with Prof. Morley that drainage should not be carried out in a wide general peritonitis; in fact, any local drainage in a widespread infection was almost a waste of time, but he would have thought that a localized abscess should be drained every time. In the presence of an abscess they drained not for the pus they found to-day but for the pus expected to be there to-morrow. In all conditions the forestalling of ileus was one of the most important things to be done. He endorsed what had been said in criticism of the Fowler position. The position was based on "nursery mechanics," and had no support in physiology or animal experiment. Prof. PATERSON ROSS raised the question of morphine in acute cases. It was often taught that a well-localized peritonitis could quite safely be treated by morphine; but it was not safe with a diffuse peritonitis. He could not help thinking that if there was diffuse peritonitis and it was desirable to give the bowel complete rest morphine could be used both with safety and benefit. He added his condemnation of Fowler's position. The obstruction to the return of venous blood from the lower limbs set the stage for thrombosis and increased the risk of embolism. The advantages to the circulation by not adopting the Fowler position were considerable. Mr. DICKSON WRIGHT spoke of the importance in peritonitis of the abstraction of fluid from the general body circulation. He was a great believer in the use of suction. If the body fluids could be shifted a great deal of good could be done to the patient. Mr. MARTIN said that he invariably used morphine in acute peritonitis and was convinced that it was life-saving. He had used it both in traumatic cases during the war and in ordinary cases following appendicitis and perforated ulcer, as it prevented distension and brought about rest. Mr. DONALD asked whether Prof. Morley would differentiate between children and adults in the matter of drainage, remembering the old adage: "When in doubt with an adult, do not drain; when in doubt with a child, drain." Mr. SOLLY COHEN asked whether there was any danger in giving blood rather than plasma. Was the increased cell concentration dangerous? He wanted a reasonable explanation of what was meant by peripheral circulatory failure. Again, what penicillin dosage should be given? Which type of sulphonamide was most useful given by mouth? What was meant by the term "splanchnic reflex"? He doubted whether the Fowler position itself contributed to subphrenic abscess.

Mr. ROB, in reply, said that during the war he had treated abdominal wounds both before and after the introduction of penicillin. Of 89 abdominal wound cases treated with sulphadiazine, none of which were drained, the abdominal incision became infected in 6. Of 37 treated with sulphadiazine and penicillin, all healed by first intention. On the question of blood or plasma, in his opinion blood should be used when blood had been lost and plasma when plasma had been lost, as the two fluids were not interchangeable. Prof. MORLEY said he was sure that for peptic ulcer drainage was not only unnecessary but dangerous, because it was so particularly liable to give rise to bands of adhesions. He did not attach much significance in acute cases to the blood picture. One had to depend much more on the general clinical phenomena. He was a whole-hearted believer in the use of morphine in peritonitis; the bowel needed the rest which morphine ensured.

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## FAMILY PLANNING ASSOCIATION

Some 130 doctors attended a medical conference of the association held on Nov. 24, when "the experience of some local authorities in providing contraceptive advice within the terms of the Ministry of Health Memoranda" was discussed under the chairmanship of Dr. ANNIS GILLIE. Since 1933, thanks largely to the F.P.A., the provision of advice on contraception at clinics has become a generally accepted part of the medical services, and there was great hope of further progress under the new Health Act.

Dr. MARGARET TURNER described her experiences in running one of the ten clinics provided by Essex County Council and emphasized the great need for a service which would cover fully all the aspects of family planning such as marriage guidance, sub-fertility, and the treatment of minor gynaecological ailments as well as contraception. Experience in many different types of clinics was represented in the ensuing discussion, which ranged widely over all the problems that their organization present.

### Developments in the Treatment of Sub-Fertility

With Prof. W. C. W. NIXON in the chair, Dr. MARGARET JACKSON outlined the methods and investigations that she used and made the following points: that one of the most important aspects of the clinic was to sort out the hopeless from the hopeful patients; the importance to the peace of mind of the former group of patients of knowing exactly where they stood could not be overestimated; that as fertility was greater before than after the age of 30, it was important for married couples to try to have children as early as possible so that if sub-fertile they should have a chance of successful treatment. She emphasized the importance of investigating the husband as well as the wife and illustrated the growth of her work by the fact that, whereas in 1933 0.5% of her clinic patients came for sub-fertility, the proportion is now 33%.

The conference ended with a showing of the film "Studies in Human Fertility," which was made in the United States and has been used in that country for the instruction of medical students.

# Correspondence

### Unswerving Support

SIR,—I resigned from the B.M.A. at the end of 1939 owing to a difference of opinion with an official of the Association on what I considered a matter of principle. For the past three months I have been reading the *Journal*, and am now quite convinced that not only is this not the time to perpetuate a grievance (fancied or otherwise), but that it is the proper time for every member of the profession who values his personal liberty and the welfare of his patients to give his unswerving support to the Association. I am therefore making a formal application to the Association to be readmitted to membership to-day.—I am, etc.,

London, N.19. C. H. JOHNSON.

### The Plebiscite

SIR,—I have answered "No," but I am distressed to think that my answer may be construed as having the implications referred to in the preamble of the plebiscite form. I hold that "the profession should decline to accept service under the Government scheme," but I do *not* hold this opinion "in view of the wide divergence between the principles of the profession and the provisions of the Act," for I disagree with the first four of the five decisions of the Representative Body mentioned in Dr. Hill's letter.

I approve in principle of the enactments regarding "direction," State ownership of hospitals (but not nursing homes), sale of practices, and basic salary; but my emphatic hostility is aroused by the many points—I have counted eighteen in the Act—at which the Minister may exercise an arbitrary power. To my mind the worst of these eighteen relate to his (*a*) withholding the annual report of the Central Health Services Council, and (*b*) compulsorily acquiring any medical institution which may be set up in the future. If the referendum shows a substantial majority of "Noes" I trust that the Council will not claim that this majority is unanimous in its reasons for condemning the National Health Service Act.—I am, etc.,

London, N.19. G. A. VAN SOMEREN.

SIR,—To read the correspondence in recent numbers of the *Journal* one might think that the future of the human race was at stake in the plebiscite. Your correspondents dislike the Labour Government and all that it stands for. Let them say so and have done with it but not confuse the issue by indulging in political diatribes. The fact is that the Labour Government (supported in this instance by the Liberal Party) have a clear mandate from the electorate to pass the National Health Service Act. Your correspondents forget too that all political parties and the B.M.A. have urged the creation of a free and comprehensive health service. In 1944 the plebiscite of the medical profession confirmed this general wish, and more recently the students have shown that they were largely in favour too.

We doctors now have the right to negotiate with the Minister regarding the terms of service. Shall we now behave like a lot of sulky schoolboys and refuse to have anything to do with an Act of Parliament which clearly represents the wishes of the country? One's only possible doubt in answering "Yes" is whether we are wise in putting the powers of negotiation in the hands of men who have already shown their political bias and determination not to meet the Minister in a reasonable spirit.

Is the Negotiating Committee a democratically constituted body? What say—direct or indirect—had the Service doctors? Can it or the Council of the B.M.A. be said to represent the wishes of the majority of the profession? There must be tens of thousands of members of the B.M.A. who have joined—this being the cheapest and most convenient way of securing the *Journal*—and who never attend B.M.A. meetings. The difference between the viewpoint of the B.M.A. Council and the Negotiating Committee on the one hand and that of the profession as shown by the 1944 plebiscite on the other is so marked that one is forced to conclude that the former do not really represent the opinions of the profession as a whole.—I am, etc.,

Bristol. H. B. O. CARDEW.

### Northern Ireland and the Plebiscite

SIR,—Dr. Conn McCluskey's letter (Nov. 23, p. 791) came under discussion at a Divisional committee meeting this afternoon. I am asked to take immediate steps to correct the impression which may be given. The committee has no reason to assume that Mr. Grant intends to do anything other than follow the English Act in all its major details. It should not be assumed that the alternative measures which Dr. McCluskey mentions will be acceptable to the Northern Ireland Government. All evidence points to the opinion that Mr. Grant will be compelled to follow the English Act closely. Northern Ireland practitioners should not permit themselves to be misled by any assumptions to the contrary.—I am, etc.,

Belfast. DOUGLAS BOYD,
Hon. Secretary, Belfast Division.
British Medical Association.

### The Act and Ophthalmic Treatment

SIR,—Those of us who have interested ourselves in this National Health Service during the past four or five years are amazed at the apathy of the medical profession generally in a measure like a State Medical Service, which affects their living and their mode of life. Most Divisions have held meetings to discuss this plebiscite; and I should think that the experience of other Divisions has been much the same as our own at Guildford, where 12% came to hear the views of their colleagues on this subject. Of those who came the vote was a unanimous "No," and I take it that if there had been any very keen "Yes"-men they would have come to the meeting to state their views.

The planners are already at work, and in ophthalmology major ophthalmic surgery is only to be performed at key hospitals. Smaller hospitals which may have quite considerable ophthalmic departments are to be closed, for major surgery at any rate, for no better reason than that they are small hospitals. The key hospitals are well named, for those who are already installed in what are to be the key hospitals not only have the key of their own hospitals but also intend to take the key of hospitals with which they have had previously no association, and lock the door at will. I fully realize that it is only by closing the smaller hospitals that patients could be compelled to make the long journeys to key hospitals which they have been unwilling to make in the past.

Surely this must be the writing on the wall for the whole profession; and it is quite incredible to me that doctors who may have been 20 or 30 years in practices of their own should now be willing to return to their house-surgeon days without so much as a fight.—I am, etc.

Camberley. LESLIE HARTLEY.

### The Patient's Dilemma

SIR,—Apropos the National Health Service Act, wherein we are assured that the mutual freedom of choice as between doctor and patient will be retained, how would one reconcile the fact that when a practitioner chooses to remain and practise outside the scheme his patients will not be provided with free medicines and appliances under the Act. Yet, it is presumed, these same patients will compulsorily have to pay their weekly contributions to that scheme without deriving any medical benefit from it.

Should they insist upon their rights to free medical benefits under the scheme they will presumably be advised or directed to join the list of a practitioner within the scheme. Is this consistent with the freedom of choice of a doctor by the patient?—I am, etc.,

Aldershot. D. M. RAYNES.

### National Health Service Act

SIR,—Surely no right-minded citizen, no matter what his political views—unless Fascist—could desire the B.M.A. to negotiate terms with the Minister of Health. The Act as it stands is an unscrupulous, expensive political pawn which gives the Minister dictatorial powers over the medical profession. The Socialist should bear in mind that the next Minister of Health might be a Conservative.

The expense of running this dictatorship, with its multitudinous subcommittees and boards, all ultimately appointed by the Minister, does not bear thinking about. In a country

which is on the borderline of bankruptcy it is not ludicrous but terrifying. Those prepared to use the Act as a basis of negotiation admit by implication approval of it as far as it goes. It is not a case of making the best of a bad job, but of resisting evil all along the line and having as little to do with it as possible. The idea of increasing the facilities for, and the medical care of, the country is good and perhaps overdue ; but we must not be party to a scheme which can only lead to a decrease in this ideal.

A further rather important snag in the scheme as proposed, which seems to have been overlooked at the present, is in regard to hospital accommodation. The latter is inadequate at the moment to cope with all the cases who would honestly benefit from it. In consequence many patients are treated as well as possible, and frequently with success, in their own homes, though ideally they would be hospitalized. Under the new scheme all pay equally to the upkeep and have equal right to the very best care. Therefore all these cases have the right to hospital treatment. What right has the mere doctor, an executive in a monster machine, to deter them merely because the bed situation is difficult? At the moment, because it is not a "right" for all, the doctor can and does use his discretion, even though this may throw a great deal of hard work upon him—visiting regularly the more seriously ill. The situation might become, and certainly could be made, quite impossible. —I am, etc.,

Cheam. NEVILLE K. CONNOLLY.

SIR,—A decision not to enter the National Health Service would be, according to your leading article of Nov. 16 (p. 739), "strictly legal *and honourable*" (italics mine). I entirely disagree.

The "fundamental principles" on which the B.M.A. has taken its stand are not moral principles. They are merely political, the cornerstones, in fact, of Conservative policy—private enterprise (or practice); private ownership (of practices); vital businesses (including medical practices) run as independent, competing, profit-making units, unplanned as to their location or number; and minimal "evolutionary" changes at slow tempo. But these are no longer the guiding principles of society. A Socialist administration has been freely elected to power and is committed to the nationalization of certain basic undertakings —communications (Cable and Wireless, Ltd.), banking, coal-mining, railways, and medical services.

We are entitled no doubt to vent our displeasure and disappointment to a reasonable extent, but do not let us carry opposition too far. We are citizens even before we are doctors, and we have surely a moral obligation as citizens to co-operate in putting into effect Acts passed by Parliament however distasteful to us personally. I suggest our profession should take its "medicine" in a sporting spirit and try to make a success of the National Health Service. This is probably, moreover, wise practical politics. In the event of a prolonged and bitter struggle with the Government it is we, I am convinced, who would suffer most.—I am, etc.,

Wallasey. LENNOX JOHNSTON.

SIR,—A useful purpose may now be served to forecast the present views and feelings of medical men as judged by the literature, personal contacts, local meetings, and consultant gatherings in London. As I see the position, individual opinions may be grouped into four classes.

1. Against any clause or remote threat which involves loss or possible loss of freedom. A majority, I am sure, if they are honest hold this view, but not all of them will commit themselves. A large backing of unshakable, determined men and women is essential in this category, not only to prevent the dangers of shackles, dictates, and direction, but as an example to the next group.

2. A weak collection of waverers who need guidance, further knowledge of the dangers threatening, and an assurance of their personal safety; some of these individuals are continually wondering what their colleagues in opposition practice will do instead of making up their own minds and helping the team.

3. Those who favour undiluted State service. Included here, of course, are the small Socialist group. Many of these doctors are young, have been in the Services, or may still be serving. A large number of these have seen the red light on returning home and discussing matters with colleagues, or having listened to addresses. Such men and women, fearing for their future livelihood, should be made to realize that there is a shortage of doctors and room for all in our country. Apparent Government concern for their poverty is just propaganda.

4. A necessarily small group of leaders and those in high places, whose recent expressed views are, to put it mildly, disturbing. This is a pity, as many would have liked a strong lead from such presumably well-informed quarters. This is no time for half-way measures and compromise. It does not seem possible that such people are willing to take a risk and give way on some of the principles agreed by a great majority of the rank and file. This vacillation from a position mid-way between the Government and the main loyal body of the profession is not good enough. It should be realized such is in fact the case—hence the dangers of saying "Yes" in the referendum. After the way in which the Bill has been introduced, a Bevan concoction, without advice from those expected to work it, refusal to discuss matters, a *fait accompli*, etc., surely such matters can be met only by standing firm on any point even remotely threatening future dictation. Let us hope that these important individuals, on account of their high level, will not fear to present a bolder front when the time comes.

I believe our position generally has been greatly strengthened of recent months. We hope that the quiet, unassuming Guy Dain and others will not cease their valuable addresses to groups of medical men. If they need any encouragement they might like to know that they have made many converts and assisted others to a firmer frame of mind. It may help some to know that at a recent discussion of Fellows it was obvious that the rank and file of consultants and specialists present were, as far as I could assess, wholly or almost entirely in favour of supporting the principles already laid down. I mention this because there is a growing feeling among general practitioners, whose house is now in better order, that the profession may be let down by the consultant or specialist. Meetings at the Royal College of Surgeons do not appear to support this view. Mr. Reginald Payne, Laurence Abel, and others should be thanked for their efforts at the Fellows' discussion. Mr. Payne, who has taken much trouble in studying laws, rules, and regulations, and the dangerous growing powers of the politician, should receive special thanks for his effort, and I hope he will publish his remarks. During his lengthy and necessarily dry discourse I heard a whisper behind me, "For Heaven's sake keep politics out of this discussion." Such a remark savours of much dangerous ignorance. Much as we dislike it the politics of the present Government are thrust on us and we must face, discuss, and fight the dangers inside and outside the profession.

How many doctors know the meaning and implications of the "closed shop"? Why must we wait for incidents like the Willesden Hospital staff-sacking threat before we blink our large baby blue eyes! It will be amusing to see how the Ministry of Health explain or minimize this blunder. Possibly to save face some minor official will be rapped over the knuckles. The "closed shop" is on our doorstep. Basic freedoms and minorities are daily involved in an overbearing and destructive process. The medical profession is a minority community, unassailable if we stand together. We have the opportunity; we have also a chance of perhaps setting an example and encouraging other bodies of men and women who are British to call a halt to the Britons already on the road to serfdom. We do not seem to realize the dangers, in spite of having just emerged from the world's greatest disaster—the result of a one-party dictatorship.

I cannot understand how supposedly sane professional men and women can countenance drastic changes and chances *at this particular moment of all moments* in our long and honoured medical history, while the process of aping recent Continental dictatorships is in our midst and hot-headed M.P.s will tell us when, where, and how we will do our work. I recommend this thought to everybody—even to those who would fail us in the fight for freedom.—I am, etc.,

Torquay. W. ETHERINGTON-WILSON.

## Ends and Means

SIR,—I have just received a copy of Bulletin No. 16 from the Medical Policy Association (London), which strongly urges the professions not to send a deputation to the Minister of Health to discuss with him the Health Act. I am second to none in my dislike of the Act, and the overbearing attitude of the Minister in the matter. I deplore the proposed rape of the hospitals and the twilight of the freedom of medical men as

individuals. Nevertheless, in my humble opinion a refusal to meet the Minister is playing right into his hands—it is both undignified and unwise. One can almost hear his reply—"I gave them a chance to meet me, and they sulked and would not play." It would show a pettiness that is unworthy of the profession. I believe a large section of the public would take the same view, and we cannot afford to ignore public opinion on such a vital issue.

The last paragraph but three (heavy type) leaves one bewildered, if words have any meaning. It states: "To vote for negotiation is to agree with the Minister's aims because *you cannot honestly discuss means unless you are in agreement with the ends.*" One assumes that the deputation would tell the Minister in unmistakable terms what it thinks of the Act as a whole—and of many of its clauses. How this could be construed as "agreement" passes comprehension.—I am, etc.,

London, N.20. B. HALLEY STEWART.

## Cerebral Malaria in Britain

SIR,—I read with interest the account (Nov. 30, p. 815) by Drs. J. R. Ryder and R. T. Towson of their case of cerebral malaria, which reminded me of a case seen by myself and described in the *Journal* of April 27 (p. 650). In my case the patient was completely comatose and had not had any previous recognized attack of malaria, but he did show a profound haemolytic anaemia and an enlarged spleen.

As in the case of Drs. Ryder and Towson, my patient had not long returned from W. Africa, and the onset of coma and high fever in a young man from that region roused an immediate suspicion of the presence of cerebral malaria. His condition appeared so desperate that an even larger dose of intravenous quinine (20 gr.) than that given by Drs. Ryder and Towson was employed. He made an immediate recovery, but my impression was that had effective treatment been long delayed this would not have been the case.

I reiterate these facts to support the statements in the recent case report that cerebral malaria should be considered as a possible cause of coma and that its early treatment is essential. The fact that a febrile comatose individual has not long returned from an area where malignant tertian malaria is endemic should certainly make us alert to this possibility.—I am, etc.,

Edgware. G. H. JENNINGS.

## Evaluation of Barrier Creams

SIR,—I would like to pay tribute to the article by Drs. C. G. A. Sadler and R. H. Marriott (Nov. 23, p. 769) and to their caution in presenting their conclusions. The practical use of barriers (and I think the writers would agree) is bound up with the physical and chemical factors operating in the aetiology of industrial dermatitis. One of the most neglected aetiological factors is that of friction. Often enough the causation of industrial dermatitis is not merely that of skin plus irritant, but of skin plus irritant plus friction. The element of friction is so important that certain abrasives, chemically inert, can by virtue of their physical property alone produce an eczematoid reaction. With substances chemically hostile to the skin the sites of the rash are not necessarily those places where the agent soils the skin: it is more often those soiled areas where the agent is *rubbed* into the skin. So a man whose whole forearms are bathed in irritant may only present a rash where his rolled up and soiled shirt sleeves constantly abrade his skin, or where the ulnar borders of the forearm rub against a protective apron or on a bench.

Because of this element of friction medical officers in industry must often be struck by the exact similarity from case to case where these dermatitis cases come from one particular job. The importance of this element of friction can be readily understood by computing how many thousands of times a muscular movement may have to be performed in a day's work. By virtue of this repetition a mildly irritating substance may be transformed into a potent source of dermatitis. All this is important in regard to the practical use of barrier creams for very obvious reasons, and because of these reasons it is not uncommon to see a correct barrier religiously applied proving useless.

Nevertheless, friction should not be overstressed. Dermatitis occurs where this is minimal, as in the formalin dermatitis of laboratory workers; but in this sort of case the chemical is often potent and hostile to the skin to an unusual degree. Where friction is great, chemical irritation can be minimal, but where friction is slight, chemical potency must be marked in order that a serious cause of dermatitis may arise. No doubt this is only a rough rule to which there are exceptions, but it may well be that a motion study of employees at work, with a view to minimizing wear on the skin, could often be a better answer than the application of a barrier to the skin. It is at any rate remarkable in industry that the risk of dermatitis does not necessarily run parallel with the irritating power of the substances handled. The very irritant substance may in practice be less harmful than a mild chemical because the nature of the work may be the main determinant.

The housewife might merely immerse her hands in warm alkaline solutions with impunity, but who can doubt that the element of friction on washing-day adds the final touch to the destructive power of the alkali on the horny layer? How does a barrier behave to this great but unrecognized element of friction? It seems to me an important point in very many jobs with a dermatitis risk.—I am, etc.,

Morris Motors, Ltd. G. WHITWELL.

## Penicillin and Acute Puerperal Mastitis

SIR,—Drs. Mary Taylor and Stanley Way's instructive publication on "Penicillin in Treatment of Acute Puerperal Mastitis" (Nov. 16, p. 731) has appeared most opportunely for me, as I have just finished my observations on a case of mine.

### CASE REPORT

A.B., aged 34 years, para. 2. On Oct. 23, 1946, dribbling of liquor amnii commenced, and continued with irregular short pains. Admitted into the maternity home late Oct. 27. Occipito-posterior position of the vertex, with restitution and abrupt normal termination of a tedious labour on the evening of Oct. 28. Lactation commenced Oct. 30.

Nipples cracked and breasts began to be tender on Nov. 1. Rigor and pyrexia 102° F. (38.9° C.) early hours of Nov. 3. By mid-day temperature was normal and breasts soft with no tenderness on pressure. Lactation stopped. Nov. 7: rigor and pyrexia, with flushing and exquisite tenderness of the left breast and lower half of the right breast. The patient felt and looked ill. Penicillin injections commenced Nov. 8—500,000 units twice daily till 5,000,000 units had been injected. Nov. 11: patient passed from great distress into comfort, and the breasts became soft and palpable.

Nov. 13: patient returned home and is now going about. Stilboestrol 5 mg. was administered throughout this treatment, and breasts were pumped.

The magical clearing up of both the breasts under the massive penicillin injections in so short a time is worthy of note.—I am, etc.,

Warrington. FEROZE GANDHI.

## "Benadryl" for Penicillin Urticaria

SIR,—The article by Lieut.-Col. R. R. Willcox (Nov. 16, p. 732) on the use of "benadryl" for penicillin urticaria prompts me to record a recent case in our practice in whom a similar beneficial effect has been observed in urticaria following liver injections.

This is a woman who had been having a maintenance dose of 2 ml. "anahaemin" monthly for the past five years for pernicious anaemia. In January this year she had a mild urticaria following her injection, which settled down after a few days. After her next injection in February she had a most violent and profuse attack of urticaria with oedema of the tongue, the glottis, and the eyelids—this despite the fact that 5 min. (0.3 ml.) of adrenaline was given with the "anahaemin." Once more "anahaemin" was injected with 10 min. adrenaline, but with the same unfortunate effect. After this she refused to have any more. An attempt was made to desensitize her by giving her orally minute increasing doses of proteolysed liver, but each time she reached about a teaspoonful dose the urticaria appeared again.

On Oct. 16 I was summoned to see her and found her in a state of collapse, with dyspnoea, feeble heart sounds with tachycardia, and oedema of the feet and legs. Her pallor was intense,

and she was almost moribund. From that date onwards for a fortnight she was given 2 ml. "anahaemin" daily, but at the same time she took two capsules of "benadryl," 50 mg. each t.d.s., and to my great relief and hers no urticaria appeared. For the past three weeks she has been given 2 ml. "anahaemin" twice weekly, and the dose of "benadryl" has been reduced gradually to one capsule taken after the injection only. As an experiment, on two occasions the "anahaemin" has been given without "benadryl" at all, and each time a mild urticaria of the arms and legs has appeared.

She is now very fit, and is continuing on once-weekly injections of the liver followed by one capsule "benadryl," with no untoward effects. No haematological examinations have been done on this occasion, partly for financial reasons and chiefly because the diagnosis of pernicious anaemia had been established in the past.—I am, etc.,

Bournemouth. JAMES NICHOLSON.

### Treatment of Osteoarthritis by Lactic Acid Injection

SIR,—I am grateful to Dr. R. Mawson for his article (Nov. 9, p. 691), and I envy him his power of lucid exposition and graphic description. As originator of this method of treatment I find little to cavil at, and if I differ from him in certain details of technique I hope he will not think me captious. During the last twelve years I have been responsible for the injection of approximately 10,000 cases, and this experience has led me to the following conclusions.

(1) It is a mistake to use a local anaesthetic. I use much finer needles than Dr. Mawson—e.g., for hip-joint a needle 3¾ in. (9.4 cm.) with a bore of 0.55 mm., for the knee a needle of 20 S.W.G. bore. (Incidentally, why, oh why do the manufacturers cut down the *length* of the needle with the *bore*?) I attribute my complete absence of sepsis to these two factors.

(2) I very rarely use the anterior approach to the hip-joint, for the reason that effusion in the joint (more often experienced than I had thought likely) or an excessive amount of periarticular thickening may displace the vascular packet and the femoral nerve laterally, and in stout patients the pulsation of the artery is not easily felt.

(3) For the wrist-joint proper I inject via the anatomical snuff-box: but the division of this joint into radio-carpal and ulna-triangular ligament-lunate articulations is an artificial discrimination remote from clinical reality—vide Prof. Seddon's *x*-ray movies of the wrist or the average case of atrophic arthritis, where the ulnar side of the wrist is frequently more seriously affected than the radial; and I agree with Dr. Mawson that it is frequently useful to enter the wrist-joint via the ulnar side. In any case the synovial cavity communicates on the proximal side of the triangular ligament with the inferior radio-ulnar joint, and on the distal side with the radio-carpal articulation.

(4) I believe from *x*-ray examination that if severe pain is complained of immediately after injection the point of the needle is under the periosteum or the cartilage. I have not experienced it since I formed the practice of withdrawing the needle a short distance before pushing the plunger. Deliberate infiltration of the thickened capsule does not cause undue pain.

(5) The use of acid injection in active atrophic arthritis is not recommended. My admittedly inadequate observations of the joint *p*H in this phase tend to show that it is certainly not alkaline.

The suggestion has been made repeatedly that the procaine is the active ingredient in the improvement gained: Warren Crowe, however, using acid potassium phosphate without procaine, obtained highly satisfactory results; and in any case, most procaine solutions have a *p*H figure well under 7.—I am, etc.,

Sunderland. W. GRANT WAUGH.

### Immunization against Whooping-cough

SIR,—It is very encouraging to read in the *Journal* of Nov. 9 (p. 699) that the Medical Research Council is initiating in certain limited areas, in co-operation with the medical officer of health of those particular areas, experimental inoculation against whooping-cough. Its results and conclusions will be awaited with great interest.

The following comments are from the point of view of a G.P. interested in this subject for close on 20 years. (Sugaré, H., and McLeod, J. W., *Lancet*, 1929, **2**, 165.) There is great need in this country for a more extensive study of immunization against this disease, which causes such impairment of health and loss of school attendance. Several extensive investigations of its value have now been carried out, chiefly in Denmark and the United States. Their results are very favourable and point to its successful prophylactic use.

It is suggested that facilities for active immunization against whooping-cough should be made available by the public health authorities in the same way as in diphtheria, taking into account the view that the injections should commence about the age of 6 months. Combining the injections against whooping-cough with those against diphtheria has also been used. Preliminary trials have been favourable in doses of 0.5 and 1 ml. at intervals of four weeks. This combined vaccine is now generally available. More extensive trial is required, however, before assessment of the efficacy of its prophylactic use can be established.—I am, etc.,

Leeds. H. SUGARÉ.

### The Fenestration Operation for Otosclerosis

SIR,—In the interesting article by Mr. I. Simson Hall (Nov. 2, p. 647), the passive part attributed to the *stapes*, one of the most fascinating mechanisms in the body, appears to me rather misleading.

In 1931 I challenged the theory, held at that time, that the function of the secondary membrane was limited to permitting the passage along the *scalae* of movements generated at the *fenestra ovalis*, and I give a brief summary of the main points in support of my present view. In the case of a cone, such as that of the *membrana tympani*, with its base attached to the *sulcus tympanicus* and its apex directed inwards, any movement inwards would be arrested, and its pressure sustained, by its attachment to the *sulcus*. The pressure of the apex on, and the resulting movement of, the *malleus* would represent a negligible fraction of the energy of a sound wave. I maintained that, mathematically, pressure on the interior of a cone of radiating fibres would produce movement of the apex inwards, towards and not away from the base.

Subsequently, in my little work *Hearing and Equilibrium*, I published photographs of an improved model (Figs. 1 and 2) which, in my view, demonstrated conclusively that the hypothesis was correct, and that pressure, insufficient to produce extension of the fibres, tends to convert the cone into a segment of a sphere, which expands as the pressure exceeds that strength. In the case of the *membrana tympani* the effect of the initial change is a movement of the apex and manubrium outwards towards the plane of the *sulcus*, while that of the second change is a movement in the reverse direction; movements respectively supplementing weak, and resisting excessive, movements of fluid generated at the *fenestra rotunda*. The only light pressure which would resist, instead of assisting, the outward movement would be any directly on the handle of the *malleus*; but owing to the downward direction of the inner end of the external canal and the further extension downwards of its roof, waves sweep down towards the *fossula rotunda*, across rather than against the membrane, and the short process of the *malleus* diverts pressures, which would otherwise reach the handle, on to the membrane on either side. In the middle ear the depth, direction, and position of the *fossula ovalis* protects the surface of the *stapes* from pressures created by sound waves, while not interfering with the action of the ossicles. Finally the fluid movements generated by the secondary membrane are immediately to and from the *scala tympani*; while, on the contrary, those by the *stapes* are directed across the entrance to the *scala vestibuli*, a construction which, for reasons given elsewhere, does not affect its supplementary action.

*Action of the tensor tympani.*—Waves do not penetrate the *membrana tympani*; movements in the middle ear in harmony with sound waves are generated by its deep surface. Those from its lower more vertical part are directed immediately towards the *fossula rotunda;* while those from its upper relatively more horizontal part are mainly directed to the region above the *fossula ovalis*. The *tensor tympani* responds to sound in a manner resembling the response of the iris to light. As sound becomes excessive it forces the *stapes* into the *fenestra ovalis* with

increasing strength, thus preventing excessive movement of the fluid. Simultaneously it raises the tension of the membrane, reduces the amplitude of the movements generated by sound waves and, consequently, of the movements generated by its deep surface towards the *fossula rotunda*. It would be difficult to conceive a more beautifully co-ordinated arrangement for the rapid appropriate conversion of a supplementary into a protective mechanism.

The apparatus consists of a cone of elastic tissue ribbed with comparatively inelastic material, and sealing the upper glass vessel, thus simulating the *membrana tympani* separating outer and middle ears. Two straws (B and S) lie side by side across the base of the cone, but S is hinged at H, and has a looped attachment at L to a small vertical straw resting on the apex of the cone, while A serves as a guide and an indicator for the upward movement of S. S thus simulates the *malleus*.

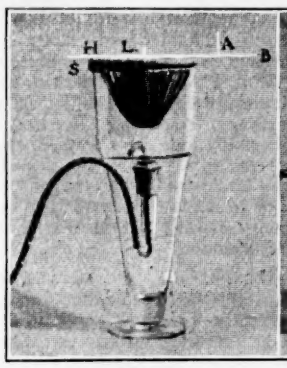


Fig. 1

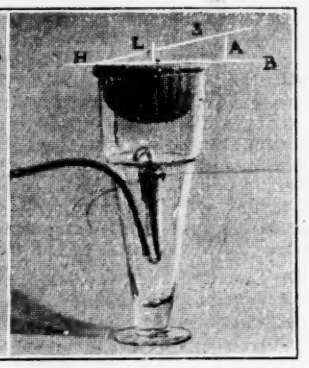


Fig. 2

In Fig. 1 the atmospheric pressures are equal on the two sides of the membrane, while in Fig. 2 the glass chamber is partially evacuated with the cone assuming a more hemispherical shape and its apex unexpectedly rising as a consequence of the inelasticity of the radiating ribs.—I am, etc.,

H. MACNAUGHTON-JONES.

### Facial Palsy Accompanying Acute Mastoiditis

SIR,—With regard to Mr. Arthur Miller's letter (Sept. 28, p. 474), it seems to be worth mentioning that high power magnification now enables one to view the horizontal or intratympanic portion of the facial canal much more clearly than before. The pinkish-yellow nerve appears to be very thinly covered by bone, so thin in fact that one suspects that an actual dehiscence is present, only to find that there is a covering of very transparent bone. Personally I am surprised that facial palsy is not more common when the tympanic cavity is the site of severe inflammatory changes.—I am, etc.,

London, W.1. IAN G. ROBIN.

SIR,—May I comment upon the sulphonamide treatment of Case 4 of facial palsy accompanying acute mastoiditis as reported by Dr. Kenneth R. Ogilvie (Aug. 24, p. 263), as this is a matter of considerable importance. The history as reported gives no information as to the onset or duration of the preliminary attack; and apparently, although otorrhoea was present, the only treatment was "a sulphonamide—2 g. daily for five days."

It is a golden rule in cases of otorrhoea that the ear must be kept "clean and dry," and this suffices for the great majority of cases—at least in this part of the world. With regard to sulphonamide therapy, it is unfortunate that indiscriminate and ill-informed use of sulphonamides is so widespread. Sulphonamides are not without their dangers, but it must be realized that insufficient dosage is worse than useless, for not only does it fail to cure but it does develop resistance to sulphonamides in organisms that are otherwise susceptible, and may lead to a false sense of security. I consider it wrong and dangerous to give sulphonamides to ambulatory patients.

In the case in question 2 g. daily for five days was a totally inadequate dosage, and from the information given was probably administered not early enough. In cases of acute otitis media the administration of sulphonamides must be in adequate dosage, be commenced early, be conducted with the proper safeguards, and under careful supervision. Neglect to observe these conditions has been responsible for much unwarranted criticism of the use of these drugs in acute otitis media. To reserve chemotherapy for "cases which show a tendency to spread outside the mastoid process . . . " is to subject many patients to the risk of operations, illness, and expense which could be avoided by early and sufficient intelligent care.—I am, etc.,

Brisbane. ERNEST CULPIN.

### Transmesenteric Hernia

SIR,—The recent correspondence on this relatively uncommon subject has produced interesting differences of opinion concerning its aetiology. As I recently had the opportunity of operating on one of these cases I would like to add my support to the view of its congenital origin so well stressed by Mr. E. G. Dolton (Nov. 2, p. 667).

In my case there was a history of apparently intermittent obstruction extending over a fortnight, and the patient when seen was *in extremis*. There had been no history of abdominal injury. At operation it proved impossible to reduce the prolapsed small gut, and as the obstructing twist was seen in the terminal two inches (5 cm.) of the ileum and was not gangrenous, a rapid lateral anastomosis between the lower portion of the distended ileum and the caecum was done. Unfortunately, on completion of the operation, a tragedy supervened. The patient vomited violently and aspirated a quantity of vomitus, dying in a few moments despite all attempts at aspiration and cardiac massage, etc. I should add that the stomach had been emptied and spinal analgesia employed, but it was found necessary to supplement this by inhalation anaesthesia.

At the subsequent necropsy it was found that the opening in the mesentery measured four inches (10 cm.) at its greatest diameter and was approximately circular. Twelve feet (3.6 m.) of small gut had herniated through the opening, explaining the difficulty in attempting to reduce it at operation. But the important point was that a very careful and detailed examination of the edges of the opening was possible, and this left no doubt whatever that it was in fact a congenital development. Blood vessels of normal size ran along the free margin and anastomosed to complete the pattern before entering the gut. There was no evidence of any previous inflammatory changes and no evidence of healed blood vessels, which must have been torn if the defect had been caused by injury. The very shape of the defect—almost circular—must, I think, dispose of the possibility of trauma, since massive haemorrhage must have resulted.—I am, etc.,

Londonderry. W. V. BEACH.

### Fewer Strengths of Insulin Preparations

SIR,—Originally there was only one strength of insulin solution—20 units per ml. Now there are three strengths on our market—20, 40, and 80 units per ml. Each batch has to be carefully and expensively standardized, checked, labelled, and issued. The manufacturers and the M.R.C. carry out this long-accepted labour ingrained by pharmacopoeial regulations, and it remains for a clinician to state that it would be both helpful in practice and economical in production to omit the weakest solution—20 units per ml.

For many years my diabetic clinic and many others have never used the weakest solution—U.20—nor found it necessary. Even if an unusually small injection of under 10 units is being given, it can be measured accurately enough in U.40 strength. In doses of over 10 units U.40 should always be used for the benefit of small-bulk injections. For the same reason, for still larger doses U.80 should be used instead of U.40.

Mistakes in insulin dosage are all too frequent and would be minimized with only two strengths. Other countries have been worse off, and the Americans have produced 10, 20, 40, 80, and 100 units per ml. strengths. They now propose only two—40 and 80 units per ml. Surely there will be unanimity over this simple suggestion. The clinicians give their blessing, the M.R.C. and the *Pharmacopoeia* add theirs and change the regulations, the manufacturers bless everybody and act quickly —I hope.—I am, etc.,

King's College Hospital, S.E.5. R. D. LAWRENCE.

# Obituary

## J. SHAW BOLTON, M.D., F.R.C.P.

After a long illness Dr. Joseph Shaw Bolton died on Nov. 12 at his home at Beaconsfield. He was born in 1867, son of the late Isaac Bolton, of Whitby, and elder brother of Dr. Charles Bolton, F.R.S. He was educated at Spring Hill School, Whitby, close to which his home was, and went on to University College, London, and to the medical school of University College Hospital. He took the degrees of B.Sc. in 1888, and of D.Sc. in 1912. In 1894 he qualified as M.B., B.S.Lond., with a gold medal in medicine, and proceeded to M.D. the following year. He became M.R.C.P. in 1902 and F.R.C.P. in 1909—to the latter distinction he was admitted on the same day as his brother, which one would suppose must surely be a unique event. He also received an honorary D.Sc. from Leeds University in 1934. At University College he was Atchison Scholar, Filliter Exhibitioner, and Fellow of the College. After qualifying he was demonstrator of anatomy at his own hospital, and lecturer on physiology at Mason's College, Birmingham, in 1897–9. He was then appointed assistant medical officer and pathologist to the L.C.C. asylum at Claybury, and remained in the mental hospital services for the rest of his career. He was at Hellingly 1903–5, at Rainhill 1905–10, and was then appointed superintendent at Wakefield, where he remained until his retirement in 1933. He was also professor of mental diseases at Leeds University from 1911 to 1934.

Shaw Bolton was a tireless worker and a prolific writer, whose reputation was firmly established by his publication (in 1914) of *The Brain in Health and Disease*; he had then already to his credit the Goulstonian Lecture for 1910 on "Localization of Cerebral Function," and in 1935 he was Lumleian Lecturer to the College of Physicians on "The Evolution of Mind." He was also Maudsley lecturer in 1925, Henderson Trust lecturer in 1933, and author of monographs in Quain's *Dictionary of Medicine*. He was on the Council of the R.C.P. 1928–30, and President of the Royal Medico-Psychological Association in 1928. Such a record speaks for itself; and if he was not in sympathy with some of the more extravagant psychiatric speculations, it is yet to be proved that he was wrong. Even when immersed in the administrative duties of a very large mental hospital he found time to continue his pathological work, in which his researches were of real value. At the same time he had the gift of training his staff and of imbuing them with his own enthusiasm; many of his junior medical officers have subsequently risen to eminence in psychiatry. In 1906 Shaw Bolton married Miss Ellen Rogers, who survives him with their three children, two of whom—their daughter Marjorie and their son Reginald—are also members of the medical profession.

An old colleague writes:

His home life was a perfect example of domestic harmony and delightful simplicity, and to be a guest at his house was a most enjoyable experience. Content for himself with very simple fare, he encouraged without stint or limit the most gay and liberal hospitality, and although himself an abstainer he took pride and pleasure in the care of an excellent wine-cellar for the entertainment of his many friends. To know him well was to love him, and to some of his personal admirers it seemed sometimes unfortunate that the quite extraordinary charm of his personality was, by his retiring habits, concealed from the world that knew him only through his scientific work. He scorned to display this work with an eye to kudos or reward; and generously allowed those working under his direction to take full credit for research that would have been impossible without his guidance. Otherwise he might have attained even higher honours than he received. To his pupils and assistants he was a wonderful man, to whom they owed an irredeemable debt. In his home, to his own family, he was nothing more nor less than just Dad.—J. I. R.

WILLOUGHBY HENWOOD HARVEY, M.A.Cantab., M.D.Toronto, who died on Oct. 7, was a well-known figure in Cambridge. Born in Canada in 1881, he had several medical ancestors, some of whom practised in the backwoods of Ontario in early days. Harvey came to England and studied at Bart's in the first decade of the century, graduated M.B. at the University of Toronto in 1904, and subsequently entered Christ's College, Cambridge, as a research student in pathology, acquiring his M.A. degree by research. He held in succession almost all the research scholarships available, first a B.M.A. Scholarship and then the Beit, Grocers Company's, and John Lucas Walker Fellowships. During this time his work was mostly histological in connexion with arteriosclerosis, and he published in Virchow's Archives on experimental bone formation in blood vessels. For some years he worked with the late Prof. W. E. Dixon in pharmacology, demonstrating that excessive tea and coffee produced nephritis in rabbits; at one time he was excited to discover muscle in the kidney, only to find that it had been demonstrated long since and never got into the textbooks. In the war of 1914–18 he was captain, R.A.M.C., in charge of a central V.D. laboratory in Cambridge, and was later a Secretary of that Section at the B.M.A. Annual Meeting there in 1920. For some years he lectured on immunity to the D.P.H. classes. Nothing would ever persuade Harvey to consider leaving his beloved Cambridge, but family needs made him give up pure research and take up clinical pathology, which he practised for the rest of his active life, being bacteriologist to the borough and county of Cambridge; but he remained a research man at heart. He had an original, unworldly mind, and like a true pioneer he always questioned the axioms.

Dr. STUART ERNEST GORDON, who died on Nov. 18, was born in Dublin on Oct. 17, 1889, son of the late Alexander Gordon, L.R.C.P. He was educated at St. Andrews and Wesley Colleges, Dublin, and studied medicine at the School of the Royal Colleges of Physicians and Surgeons. After qualifying in 1915 he held resident posts at the Newcastle Sanatorium, Co. Wicklow, and at the Norwich City Asylum, Norfolk. He was in general practice for a time and then took up tuberculosis work at the Middleton-in-Wharfedale Sanatorium, Ilkley, and at the Ashover Sanatorium near Chesterfield.

Dr. C. Thackray Parsons writes: The first reaction of many of HARRY ROBERTS'S intimate friends to the broadcast announcement of his death must have been the same as mine —"It is impossible." We knew how precarious his hold on life was, but it seemed as if his personality, will, and mental activity were keeping death at bay and might continue to do so. His was a full life, full of many activities and many achievements. He had a passionate love for freedom and for humanity. A lifelong Socialist, he dreamed of a Commonwealth organized to produce at the least possible cost in distasteful work and leaving each member free to live his own life in his leisure. He was friends with all men, but he sought most those who were unusual and unconventional, if they were free from pretence. He assumed a veil of cynical humour which failed to hide the warmth of his feeling for all who were wounded in the struggle of life, and for what he held to be righteous and true. His energy was inexhaustible. What he did in the East End of London, in Petersfield, and in Hawkley brought him hosts of friends and of workers who looked to him for guidance. He has left a memory that will endure. An original thinker, his mind stored with the best in literature, he was able to clothe his thoughts in words of beauty and force both in his writings and in his talk. He loved to gather friends around him, to interchange thoughts and discuss problems. With his clear and logical mind he was quick to seize upon a fallacy in an argument and to expose it mercilessly and wittily without leaving any aftertaste of bitterness. His life was an inspiration, and when so many charmed memories remain there is no death.

The following appreciation of Dr. WILLIAM HENRY PEACOCK comes from Prof. R. M. Gordon: The loss sustained by the Colonial Medical Service through the death of Dr. Peacock has already been recorded in the *Journal*. The announcement of his death will have been read with sorrow by all who have interested themselves in furthering medical projects in West Africa. It was characteristic of the man that his help and kindliness extended far beyond his official duties, and reached out to all who, like himself, were interested in alleviating suffering. It was in this way that each newcomer to the Sir A. L. Jones Research Laboratory (of the Liverpool School of Tropical Medicine) in Freetown came to know and trust Peacock, and to appreciate his sound common sense, his very considerable medical knowledge, his gift of foreseeing and eliminating obstacles both official and unofficial, and above all his loyalty and devotion not only to the Service in which he worked but to the profession which he so finely represented.

# Universities and Colleges

## UNIVERSITY OF CAMBRIDGE

Sir Edward Mellanby, K.C.B., M.D., F.R.S., Secretary of the Medical Research Council, has been elected into an Honorary Fellowship of Emmanuel College.

At a Congregation held on Nov. 16 the following medical degrees were conferred:

M.B., B.CHIR.—N. H. Harwood-Yarred and W. A. A. Hodges (by proxy); H. G. Mather (in person).

## UNIVERSITY OF LEEDS

At a meeting of the Council, held on Nov. 27, the Pro-Chancellor drew attention to the recent losses by death of two emeritus professors—J. Shaw Bolton and T. Wardrop Griffith—and referred to the valuable services which they had given to the University as professors for twenty-two and thirty-eight years respectively.

Dr. R. N. Tattersall was appointed full-time lecturer in medicine, and Dr. D. Taverner tutor in medicine.

## UNIVERSITY OF MANCHESTER

The Council has appointed Alexander Michael Boyd, F.R.C.S., as full-time Professor of Surgery and Director of the Department of Surgery, from Dec. 25.

## UNIVERSITY OF EDINBURGH

Prof. R. J. Kellar, F.R.C.S.Ed., F.R.C.O.G., who has succeeded Prof. R. W. Johnstone in the University Chair of Midwifery and Diseases of Women, gave his inaugural lecture on Nov. 14 in the Pollock Memorial Hall, with the Principal, Sir John Fraser, in the chair. Discussing the modern trend of maternity hospitals Prof. Kellar expressed the view that some 75% of all women in urban areas would be delivered in institutions, and any calculation of future needs in maternity accommodation must use this as a minimum figure. It might be taken as an axiom that a maternity hospital was out of date in many of its features within a decade of its construction, and he recalled that Sir J. Y. Simpson had seriously proposed burning a maternity hospital every few years to rid it of puerperal infection. Prof. Kellar said that Edinburgh might be regarded as the birthplace of antenatal care. But notwithstanding the saving of lives each year most of them were extremely dissatisfied with certain aspects of the antenatal clinic. This must become in future more of a social centre, where the patient could receive not merely a brief intensive abdominal examination, but also instruction in elementary hygiene, in preparation for delivery, and in infant management. More antenatal beds were needed. Again, the time might be ripe for setting up some central organization to deal with all the problems of abortion, stillbirth, infertility, and population trends. Child guidance and marriage guidance clinics would have much to gain in association with such a group, which might well be a subdivision of the Department of Social Medicine. The managers of the Edinburgh Royal Infirmary had allotted accommodation for a clinical research laboratory within the precincts of the Maternity Hospital, and this might well work in conjunction with the new extended University Department.

## UNIVERSITY OF GLASGOW

Sir John Boyd Orr, M.D., F.R.S., has been elected Chancellor of the University of Glasgow. The election was conducted by postal ballot and resulted in 6,113 votes for Sir John Boyd Orr and 5,420 for Sir Iain Colquhoun.

## ROYAL COLLEGE OF SURGEONS OF ENGLAND

*Primary F.R.C.S. Examination Overseas*

The Council of the Royal College of Surgeons of England, having acceded to requests from the Royal Australasian College of Surgeons, from the medical faculty of the Egyptian University, Cairo, and from the Director-General of Medical Services in India, to conduct the Primary F.R.C.S. examination overseas, has appointed the following examiners for this purpose: Sir Heneage Ogilvie, Prof. B. A. McSwiney, F.R.S., and Prof. G. Hadfield. They will conduct the examination in Cairo, Madras, Melbourne, Sydney, and Dunedin, beginning in Cairo on Dec. 12, in Madras on Dec. 23, and in Australasia on Jan. 6. The examiners should arrive back in this country about the end of January.

The extent to which the facilities thus offered to those medical graduates of recognized universities and colleges overseas are appreciated may be indicated by the numbers who have entered for the examination at the several centres: Cairo, 32; Madras, 65; Melbourne, 63; Sydney, 29; and Dunedin 35, a total of 224 candidates. In due course those candidates who satisfy the examiners will be eligible to appear for the final F.R.C.S. examination in this country, and will have the opportunity of studying surgical practice in England.

The following associate examiners have been appointed to assist the examiners: In Cairo, Prof. D. E. Derry and Prof. G. V. Anrep, F.R.S. In India, Prof. A. Ananthanarayana Iyer. In Melbourne, Prof. S. Sunderland. In Sydney, Mr. Douglas Miller. In Dunedin, Mr. John Cairney.

A course of 72 lectures in anatomy, applied physiology, and pathology will begin at the College on Feb. 3, 1947, and will continue until March 28. There will be two lectures daily (Monday, Tuesday, Wednesday, Thursday, and Friday) at 3.45 p.m. and 5 p.m. The fee for the whole course is £15 15s. Fellows and Members of the College and licentiates in dental surgery will be admitted on payment of a fee of £10 10s. It will not be permissible to take one or two subjects only. Applications, accompanied by a cheque for £15 15s. or £10 10s., should be sent to the assistant secretary, Royal College of Surgeons of England, Lincoln's Inn Fields, W.C.2.

Practical demonstrations in anatomy, applied physiology, and pathology have been arranged by Profs. F. Wood Jones, John Beattie, and R. A. Willis, and will be given from Monday, Jan. 6, to Friday, March 28, 1947, from 10 a.m. to 1 p.m., and from 2 to 3.30 p.m. daily. The fee is £21, and the closing date for applications is Dec. 16. The demonstrations will be open to those attending the main course of lectures to be held in Feb. and March and will be limited to 40 students, preference being given to those unable to obtain practical instruction elsewhere and to ex-Service men. Applications, accompanied by a cheque for £21, should be sent to the assistant secretary, Royal College of Surgeons of England, Lincoln's Inn Fields, W.C.2.

# The Services

Surg. Rear-Admiral J. A. Maxwell, C.B.E., C.V.O., R.N., has been appointed an Honorary Surgeon to the King in succession to Surg. Rear-Admiral H. R. B. Hull, R.N., who has been placed on the retired list.

Surg. Capt. Lambert C. Rogers, and Surg. Lieut.-Cmdrs. C. M. Lamont and A. B. Bateman, R.N.V.R., have been awarded the R.N.V.R. Officers' Decoration.

Surg. Capts. D. A. Pritchard and L. Lockwood, M.V.O., D.S.C., R.A.N., have been appointed Honorary Physician and Honorary Surgeon to the King, respectively.

Lieut.-Col. J. Morrison, O.B.E., M.C., and Major H. Mannington, R.A.M.C., have been awarded the Efficiency Medal (Territorial).

Capts. J. H. Annan and G. McL. Gorrie, R.A.M.C., have been mentioned in dispatches in recognition of gallant and distinguished services in the field.

Col. J. F. O'Grady, T.D., R.A.M.C., T.A., to be Honorary Colonel, 42nd (East Lancashire) Division, R.A.M.C., in succession to Col. A. M. Johnson, C.B.E., M.C., T.D., R.A.M.C., T.A., deceased.

Capt. T. R. Subramanaim, I.A.M.C., has been appointed M.B.E. (Military Division) in recognition of gallant and distinguished services in S.E. Asia.

## CASUALTIES IN THE MEDICAL SERVICES

*On or after Oct. 18, 1942, while a prisoner of war in Japanese hands.*—Capt. James Walsh Lillico, I.M.S.

Flying Officer CHARLES KING ALLAN, R.A.F.V.R., who was killed in a flying accident on Nov. 7, was born in December, 1922, studied medicine at Glasgow University, and qualified M.B., Ch.B., in 1945.

## AIRBORNE MEDICAL SOCIETY

It has been decided to enlarge the membership of the Airborne Medical Society, the formation of which was announced in the *Journal* of Aug. 24 (p. 282), to include all medical and dental officers who are eligible for membership of the Airborne Forces Club. That, in fact, includes all medical and dental practitioners whose business it was or is to go to war by parachute or glider. Quartermasters and transport officers of airborne field ambulances are also eligible. Application forms may be obtained from the honorary secretary, Airborne Medical Society, 63a, Belsize Park Gardens, London, N.W.3.

The Ministry of Health announces in Circular 193/46 the removal of restriction on the engagement of chiropodists, physiotherapists, radiographers, hospital almoners, pharmacists, dispensers, and psychiatric social workers; and the procedure for securing staff in these categories.

# Medical Notes in Parliament

The National Health Service (Scotland) Bill was presented by Mr. Westwood on Nov. 26 and was read a first time. The Bill had already been formally introduced and printed late last session.

### Medical Unemployment

Answering Mr. SOMERVILLE HASTINGS on Nov. 28, Mr. BEVAN regretted that he did not know how many ex-Service doctors were unable to obtain employment in general practice. Ex-Service general practitioners could take hospital posts and refresher courses available under the Government's post-graduate scheme. It was then open to them to buy or open a practice or to seek assistantships or other appropriate employment in the usual way until the National Health Service Act came into operation. He was aware that there was at present a difficulty in doctors obtaining assistantships. It was a difficulty which always arose immediately before great changes. The Ministry of Health was doing its best to mitigate the hardships where it could.

### Temporary Registration

Mr. BEVAN, on Nov. 28, told Sir HENRY MORRIS-JONES that he and Mr. Ede were consulting about temporarily registered alien doctors. He was not yet in a position to make a statement. There was no provision for temporary registration of alien dentists apart from a few practising solely by virtue of temporary medical registration. Those admitted to the dentists' *Register* had secured admission in the ordinary way. He imagined that under the new National Health Service Act all persons who were competent to practise would be competent to enter.

### Penal Reform

Replying on Nov. 27 to a debate in the House of Lords on penal reform, the LORD CHANCELLOR, Lord Jowitt, said the comprehensive Bill of 1938 would need to be reconsidered by the present Government. It was impossible to introduce this Bill this session, but he thought it was almost certain to be one of the major Bills introduced next session. The Government would use the interval in pressing ahead with probation and Borstal treatment.

Lord TEMPLEWOOD, in his introductory speech, said that during the war years young offenders under 17 had increased by 55%. In offenders between 17 and 21 the increase had been 52%, and in offenders over 21 it had been 2%. Comparing 1938 with 1945, crimes against the person had increased from 1,583 to 2,459, and sexual offences from 2,321 to 3,228. Offences committed by women had more than doubled during the war. Women's convictions for cruelty to children had increased from 345 to 1,170. Among young delinquents offences of every category by girls had gone up fourfold.

*Prescriptions for Dangerous Drugs.*—On Nov. 21 Dr. CLITHEROW asked whether Mr. Bevan knew that prescriptions for dangerous drugs and scheduled drugs were being issued to national health insurance patients in quantities sufficient, in many cases, to ensure a constant supply for many weeks—for example, 200 barbitone tablets in one case. He asked Mr. Bevan to take steps to prevent the issue of N.H.I. prescriptions containing dangerous drugs and scheduled drugs for more than one week's supply at any one time. Mr. BEVAN said that he did not think it would be proper to interfere with a doctor's discretion by any such general prohibition.

*Medical Students Not Admitted.*—Statistics given by Mr. GLENVIL HALL on Nov. 26 show that of students possessing the certificate of fitness for entrance to a Scottish University 238 made application for admission for the Session 1946–7 to the faculty of medicine, including dentistry, in Aberdeen. Of these 119, or 50%, were refused admission. Comparable figures for the same faculty were: Edinburgh 827—637, or 77%; Glasgow 760—334, or 43.9%; St. Andrews 501—398, or 78%.

*Social Surveys.*—Mr. GLENVIL HALL announced on Nov. 25 that the Social Survey of the Central Office of Information was engaged on an illness survey for the Ministry of Health, and was preparing for the Medical Research Council a report on the incidence of deafness in this country. A report was now being written for the Medical Research Council and the Ministry of Fuel and Power on the employment of miners certified as suffering from pneumoconiosis.

*Ice-cream.*—Mr. STRACHEY would like to fix a minimum standard for ice-cream but thinks this must wait until the supply of the necessary ingredients has improved.

# Medical News

*Abstracts of World Medicine* and *Abstracts of World Surgery, Obstetrics and Gynaecology* will make their first appearance in January, 1947. These two new journals are being published monthly by the British Medical Association, the first at an annual subscription of 3 guineas and the second at 2 guineas. Applications for subscription should be sent to: The Publishing Manager, *British Medical Journal*, B.M.A. House, Tavistock Square, London, W.C.1.

A joint meeting of the Food Group and the Manchester Section of the Society of Chemical Industry will be held at the Engineers' Club, Albert Square, Manchester, on Friday, Dec. 6, at 6.30 p.m., when papers will be read by Dr. N. J. Berridge on "Rennin," by Mr. H. F. Frost on "Enzymes in the Food Industry," and by Mr. S. Hilton on "Soft Curd Milk." Time will be allowed for discussion.

The fourth quarterly meeting of the Franco-Anglo-American Medical Society will be held at 11, Chandos Street, Cavendish Square, W., on Tuesday, Dec. 10, at 2.30 p.m., with Lord Horder, president of the British Section, in the chair.

A meeting of the Nutrition Panel of the Society of Chemical Industry will be held at the Chemical Society's rooms (Burlington House, Piccadilly, W.) on Wednesday, Dec. 11, at 6.30 p.m., when Mr. D. P. Hopkins will read a paper on "Fertilizers, Manures, and Nutrition." A discussion will follow. Members of the Agriculture and Food Groups are invited to attend.

A meeting of the Middlesex County Medical Society will be held at Redhill County Hospital, Edgware, on Thursday, Dec. 12, at 4 p.m., when there will be clinical demonstrations.

Sir Arthur MacNalty will deliver the FitzPatrick Lectures at the Royal College of Physicians of London, Pall Mall East, S.W., on Tuesday, Dec. 10, and Thursday, Dec. 12, at 5 p.m. The subject will be the History of State Medicine in England: (1) From the Accession of Queen Victoria to the General Board of Health, (2) The Medical Department of the Privy Council.

Mr. W. Rowley Bristow will deliver the Robert Jones Memorial Lecture on "Injuries of Peripheral Nerves in Two World Wars" before the Royal College of Surgeons of England (Lincoln's Inn Fields, W.C.) on Thursday, Dec. 12, at 5 p.m.

A sessional meeting of the Royal Sanitary Institute will be held at the Baths Hall, Legh Street, Warrington, on Friday, Dec. 13, at 10.30 a.m., when papers will be read by Dr. S. F. Allison on "The Welfare of Old People" and by Dr. J. E. Nicole on "The Mental Health of the Elderly."

The Medical Society of London announces that Sir James Chadwick will deliver the Lloyd Roberts Lecture at 11, Chandos Street, W., on Monday, Dec. 16, at 8.30 p.m. Subject: "Atomic Energy."

A meeting of the Eugenics Society will be held at the Royal Society's rooms (Burlington House, Piccadilly, W.) on Tuesday, Dec. 17, at 5.30 p.m., when Dr. J. W. B. Douglas will speak on "Social and Economic Problems of Child-bearing in Britain: Report of a Questionary Inquiry." All interested in the subject are invited to attend the meeting.

Sir Alexander Fleming, F.R.S., will give a talk on "Penicillin in General Practice" before the Paddington Division of the B.M.A. in the Inoculation Department of St. Mary's Hospital, W., on Thursday, Dec. 19, at 8.30 p.m. Members of other Divisions are invited to attend the meeting.

On Nov. 7 Mr. de Valera introduced in the Dail a Bill to establish two new Ministries for Eire—a Ministry of Public Health and a Ministry of Social Welfare.

In future, hospitals and members of the medical profession should address all inquiries concerning laboratory chemicals to the British Drug Houses Ltd., B.D.H. Laboratory Chemicals Group, Poole, Dorset (Tel.: Poole 962; telegrams: Tetradome Poole), and *not* to the British Drug Houses Ltd., Graham Street, London, N.1.

Dr. V. Puddu, Director of a Rome clinic for rheumatic and heart diseases, is visiting this country on behalf of the Italian Ministry of Health to study British arrangements for treating rheumatism and heart diseases, particularly in children's hospitals.

Dr. Joaquim Paiva Chaves, a Lisbon surgeon, is visiting Britain to study problems of traumatic surgery under Sir Reginald Watson-Jones at the London Hospital, and to visit other hospitals to see general traumatic and repair surgery. The British Council has assisted in arranging his programme.

Fifty doctors from London and Southern England were recently entertained by the Southern Railway at a luncheon in London in recognition of their help in instructing railway ambulance workers.

At a meeting of the executive committee of the Anglo-Soviet Medical Council on Nov. 13 the hon. secretary, Dr. D. E. Bunbury, reported on the present position. Throughout the year copies of British medical journals have been sent regularly to the Soviet Union by the Council. The British Council also sent 50 copies of each issue of the *British Medical Bulletin*, and a member of its staff is resident in Moscow. Soviet journals for the A.S.M.C. have been arriving irregularly throughout the year. These have been housed at the Royal Society of Medicine and have been presented to the Society's library when the Council has finished with them. Journals have been made available to the editors of the British medical abstract journals. The World Medical Association, which was formed during the year on the initiative of the British Medical Association, should be able to take over the broadest aspects of the Council's work in relation to the Soviet Union, as with other countries. The Society for Cultural Relations with the U.S.S.R. is willing to deal with specific inquiries concerning Soviet medicine, and might form a medical section with functions similar to its existing scientific and other sections. After consideration of all aspects of the present position, the executive committee decided to make recommendations to the Council for adoption at the fifth annual general meeting, to be held on Dec. 9, at 5 p.m., at 1, Wimpole Street.

The first meeting of the Pharmaceutical Liaison Committee, set up in July, 1946, to improve contact between the Ministries of Health and of Supply and the pharmaceutical profession, was attended by representatives appointed permanently from the Pharmaceutical Society, the British Pharmacopoeia Commission, the National Pharmaceutical Union, the Wholesale Drug Trade Association, and the Pharmaceutical Export Group on the one hand, and of the Ministry of Health, the Department of Health for Scotland, the Ministry of Supply, Ministry of Food, the War Office, the Admiralty, and the Air Ministry on the other.

The result of the Scottish Universities by-election was announced on Nov. 29. The Right Hon. Walter Elliot (Conservative) was returned to Parliament with a poll of 22,152 votes.

Dr. William Russell Cooper, of Clifton, Bristol, left £16,317. He left £500 to the University of Bristol, upon trust, the annual income to be paid to the medical student considered to be the most proficient at anaesthetics. After other bequests to medical friends and £300 to the Cancer Hospital, London, he had left the residue of his property to Bristol General Hospital, but by codicil dated Oct. 17, 1945, he altered this, saying, "the Government being about to take over the management of the said hospital should be responsible for its upkeep."

## EPIDEMIOLOGICAL NOTES

### Discussion of Table

In *England and Wales* infectious diseases increased in prevalence. Rises were recorded in the incidence of measles 395, whooping-cough 106, acute pneumonia 24, and diphtheria 16; the only falls were in the notifications of scarlet fever 30 and cerebrospinal fever 16.

The largest increases in the returns for measles were Durham 118, Lancashire 86, Yorkshire West Riding 56, Middlesex 43, Devonshire 42, and Dorsetshire 40. The largest fluctuations in the local incidence of whooping-cough were increases in Yorkshire West Riding 34, Lancashire 29, and London 25. The chief changes in the notifications of diphtheria were a rise in Lincolnshire 10 and a fall in Lancashire 14. Cases of paratyphoid fever were notified in Yorkshire West Riding, Sheffield C.B. 14, and in Glamorganshire 6. London, with an increase from 13 to 23, provided the only appreciable change in the incidence of dysentery; 14 of the cases were notified in Islington.

In *Scotland* increases were recorded in the notifications of whooping-cough 48, measles 32, acute primary pneumonia 32, and diphtheria 9. Decreases were reported for scarlet fever 46 and dysentery 26. The rise in the number of cases of diphtheria was due to an increase from 68 to 80 in the Western Area.

In *Eire* there were 18 fewer cases of diarrhoea and enteritis and 39 more cases of whooping-cough. The two large centres of infection for whooping-cough were Co. Laoighis, Mountmellick R.D. 40 and Dublin C.B. 21.

In *Northern Ireland* increases occurred in the notifications of measles 20 and diphtheria 7 and a decrease was reported for whooping-cough 11.

### Week Ending November 23

The notifications of infectious diseases during the week in England and Wales included: scarlet fever 1,402, whooping-cough 1,773, diphtheria 319, measles 5,428, acute pneumonia 708, cerebrospinal fever 43, dysentery 69, acute poliomyelitis 16, paratyphoid 20, typhoid 3.

No. 46

## INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Nov. 16.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

*Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for:* (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

| Disease | 1946 | | | | | 1945 (Corresponding Week) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | (a) | (b) | (c) | (d) | (e) | (a) | (b) | (c) | (d) | (e) |
| Cerebrospinal fever | 30 | 4 | 22 | — | 1 | 36 | 2 | 12 | 4 | 1 |
| Deaths | | 2 | 3 | | | | — | 1 | | |
| Diphtheria | 330 | 27 | 97 | 29 | 13 | 646 | 50 | 183 | 91 | 15 |
| Deaths | 7 | — | — | | — | 11 | 2 | 2 | 1 | — |
| Dysentery | 70 | 23 | 22 | — | — | 180 | 37 | 54 | 1 | — |
| Deaths | | | | | — | | | | — | — |
| Encephalitis lethargica, acute | 3 | — | — | 1 | — | — | — | — | — | — |
| Deaths | | — | | | | | — | | | |
| Erysipelas | | | 47 | 5 | 4 | | | 51 | 9 | 2 |
| Deaths | | — | | | | | — | | | |
| Infective enteritis or diarrhoea under 2 years | | | | 41 | | | | | 50 | |
| Deaths | 63 | 6 | 10 | | 2 | 34 | 2 | 16 | 11 | 1 |
| Measles* | 4,382 | 141 | 263 | 57 | 43 | 403 | 35 | 92 | 118 | 1 |
| Deaths | 1 | — | 1 | | — | 1 | — | — | — | — |
| Ophthalmia neonatorum | 60 | 4 | 20 | — | — | 54 | 5 | 19 | — | — |
| Deaths | | | | | | | | | | |
| Paratyphoid fever | 26 | 1 | — | 1 (B) | — | 1 | — | 2 (B) | — | — |
| Deaths | — | — | — | | — | — | — | — | — | — |
| Pneumonia, influenzal | 625 | 49 | 10 | 3 | 6 | 420 | 31 | 9 | 4 | 2 |
| Deaths (from influenza)† | 16 | 3 | 2 | | — | 14 | 2 | 2 | — | 1 |
| Pneumonia, primary | | | 308 | 31 | | | | 148 | 15 | |
| Deaths | | 51 | | | 7 | | 18 | | 12 | 10 |
| Polio-encephalitis, acute | 2 | — | | | | 3 | — | | | |
| Deaths | | — | | | | | — | | | |
| Poliomyelitis, acute | 15 | 1 | 4 | 7 | 1 | 32 | 1 | 1 | 1 | — |
| Deaths | | — | | | | | — | | | |
| Puerperal fever | | 5 | 25 | | — | | 2 | 13 | | — |
| Deaths | | | | | | | | | | |
| Puerperal pyrexia‡ | 141 | 13 | 17 | 3 | 2 | 125 | 12 | 16 | — | — |
| Deaths | | — | | | | | — | | | |
| Relapsing fever | — | — | | | — | 1 | — | | | — |
| Deaths | | | | | | | | | | |
| Scarlet fever | 1,293 | 81 | 273 | 26 | 42 | 1,674 | 134 | 269 | 19 | 42 |
| Deaths | 1 | — | — | | — | — | — | — | — | — |
| Smallpox | — | — | — | — | — | 3 | 3 | — | — | — |
| Deaths | | | | | — | | | | — | — |
| Typhoid fever | 7 | — | — | 2 | 3 | 1 | — | — | 8 | 1 |
| Deaths | — | — | — | | — | — | — | — | — | — |
| Typhus fever | — | — | — | — | — | — | — | — | — | — |
| Deaths | | | | | — | | | | — | — |
| Whooping-cough* | 1,696 | 99 | 214 | 71 | 29 | 1,203 | 84 | 51 | 32 | 3 |
| Deaths | 9 | 1 | — | | — | 5 | 2 | — | 1 | 1 |
| Deaths (0-1 year) | 384 | 59 | 72 | | 12 | 303 | 31 | 49 | 25 | 14 |
| Infant mortality rate (per 1,000 live births) | | | | | | | | | | |
| Deaths (excluding still-births) | 4,723 | 780 | 627 | | 110 | 4,294 | 638 | 560 | 184 | 109 |
| Annual death rate (per 1,000 persons living) | | | 13·8 | | | | | 12·7 | 11·9 | |
| Live births | 8,820 | 1420 | 1091 | | 245 | 6,345 | 855 | 786 | 335 | 265 |
| Annual rate per 1,000 persons living | | | 21·9 | | | | | 15·7 | 21·6 | |
| Stillbirths | 297 | 48 | 40 | | | 174 | 26 | 30 | | |
| Rate per 1,000 total births (including stillborn) | | | 35 | | | | | 37 | | |

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

‡ Includes puerperal fever for England and Wales and Eire.

It is still not possible to publish the return of births and deaths for Eire for the weeks ended Oct. 26, Nov. 2, 9, and 16.

# Letters, Notes, and Answers

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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## ANY QUESTIONS?

### Ehrlich's Reaction in Infective Hepatitis

**Q.**—*I should be grateful for advice on the technique and interpretation of Ehrlich's dimethylaminobenzaldehyde reaction as applied to the early diagnosis of infective hepatitis.*

**A.**—The technique recommended for this test is that of Watson, Schwartz, Sborov, and Bertie (*Amer. J. Clin. Path.*, 1944, **14**, 605), in which the amount of urobilinogen is estimated in a two-hour afternoon specimen of urine, the result being expressed in units which are approximately mg. per 2 hours. Alternatively the test may be used qualitatively by adding one volume of Ehrlich's reagent (0.7 g. *p*-dimethylaminobenzaldehyde, 150 ml. concentrated hydrochloric acid, 100 ml. water) to one volume of urine, followed, immediately after shaking, by three volumes of saturated sodium acetate. A definite red colour indicates excessive amounts of urobilinogen. It is important to test only fresh specimens.

In interpreting the result it must be remembered that many febrile patients may show evidence of transient liver dysfunction with positive urobilinogen tests, and that a positive result is not therefore pathognomonic of infective hepatitis; moreover, negative tests are occasionally seen in this condition. However, urobilinuria is certainly to be expected in most cases and often occurs well before the appearance of clinical jaundice.

### T.A.B. for Children

**Q.**—*At what age should children travelling to the Far East be given prophylactic injections of T.A.B. and anti-cholera vaccine?*

**A.**—Recorded examples of typhoid fever in infants are rare, and consequently it is suggested that infants and young children possess a relative immunity to the disease and that protective inoculation is therefore unnecessary. This is probably true, but it must be remembered that special care is usually taken in preparing the food of infants who are in circumstances favourable to medical observation, and that as regards other children less favourably placed the paucity of precise observations may account for the apparently low incidence of the disease. A further argument adduced against the inoculation of infants is that there is some experimental evidence that antibody formation following inoculation in the early months of life is relatively poor. Nevertheless, since the immediate local and general reactions to inoculation usually are not abnormally severe in infants or small children, there seems little reason for not giving them such protection as may result from inoculation; consequently it is suggested that children of any age should be given prophylactic T.A.B. and cholera vaccine in appropriate doses when travelling to the Far East.

### Mepacrine Dosage for Children

**Q.**—*At what age and in what dosage should mepacrine be given (a) prophylactically, (b) therapeutically?*

**A.**—Unless a child can be protected against the bites of infected mosquitoes it would seem wise to give it a suppressive antimalarial drug, and mepacrine may be used until one of the more efficient drugs, such as paludrine, becomes generally available. The relative dose of a drug depends more upon the metabolic rate of the individual than upon age, and consequently children tend to tolerate larger doses than would be suggested by age alone.

The ratio of dosage between child and adult is not two-thirds the ratio of the child's weight to that of the adult, but is this ratio raised to the two-thirds power, and this relation may be used for calculating the appropriate suppressive or therapeutic dose of mepacrine for a child of any age.

$$\frac{\text{Dose child}}{\text{Dose adult}} \propto \frac{\text{Metabolic rate child}}{\text{Metabolic rate adult}} \propto \frac{\text{Surface child}}{\text{Surface adult}} \propto \frac{(\text{Weight child})^{2/3}}{(\text{Weight adult})^{2/3}} = \left(\frac{Wc}{Wa}\right)^{2/3}$$

Approximations worked out on the above formula, assuming a normal adult of 168 lb. (12 st. or 76 kg.), are as follows:

| | | | | | | |
|---|---|---|---|---|---|---|
| For child of weight | 10 lb. | ( 4·5 kg.) | give | 1/8 | of adult dose | |
| " | 20 " | ( 9 kg.) | " | 1/4 | " | " |
| " | 30 " | (13·5 kg.) | " | 1/3 | " | " |
| " | 60 " | (27 kg.) | " | 1/2 | " | " |
| " | 90 " | (40·5 kg.) | " | 2/3 | " | " |
| " | 110 " | (49·5 kg.) | " | 3/4 | " | " |
| " | 120 " | (54 kg.) | " | 4/5 | " | " |

### Dicoumarol for Coronary Thrombosis

**Q.**—*Has any work been done in this country on dicoumarol, which is being used in America in the treatment of coronary thrombosis?*

**A.**—There was a paper by Davis and Porter in this *Journal* (1944, **1**, 718) on the use of dicoumarol in puerperal thrombosis. It has also been used for post-operative thrombosis by Prof. Learmonth in Edinburgh. A paper by Barker, Cromer, Hurn, and Waugh (*Surgery*, 1945, **17**, 207) gives useful information about the contraindications. Several other publications on the use of this anticoagulant in coronary thrombosis have appeared during this year in American publications. I am not aware of any papers on this subject in English journals.

Dicoumarol is being used in coronary disease with the aim of preventing retrograde extension of a thrombus and consequent aggravation of the cardiac lesion, and also with the object of lessening the likelihood of multiple thrombi and other complications. A trial of dicoumarol therapy is therefore indicated when a patient is not making a quick and progressive recovery after coronary thrombosis; when there is evidence of multiple thrombosis, mural thrombus, or pulmonary embolism; and when a patient is threatened with multiple successive attacks. Before treatment is begun the prothrombin time is determined. If this is 17 seconds or less 300 mg. of dicoumarol are administered orally in one dose. This dose is repeated daily until the prothrombin time is 30 seconds. Doses of 100 or 200 mg. are given daily when the prothrombin time is between 30 and 35 seconds; above this level the dosage should be discontinued owing to the risk of haemorrhage. An attempt is usually made to pursue this treatment for about a month after the last evidence of thrombosis or embolism. No series of cases sufficiently large or controlled to judge finally the efficacy of this treatment has yet been published, but the consensus seems at this stage to be favourable.

### Deodorants

**Q.**—*What are the constituents of the usual deodorants? Are such preparations harmful if used repeatedly? Would there be any advantage in using them for pre-operative skin preparation, and, post-operatively, to prevent perspiration?*

**A.**—The majority of liquid deodorants contain one or other, or a combination, of the numerous mild astringents, such as dilute alcohol, alum, zinc sulphate, formaldehyde, dilute acetic acid, and so on, sometimes coloured and perfumed. As they are not curative but merely a symptomatic treatment for excessive perspiration they have to be used repeatedly. Except in the case of persons who are hypersensitive their repeated use does not appear to be detrimental. Most of them are only very mildly, if at all, antiseptic, and it is unlikely that there would be any advantage in using them for pre-operative skin preparation, or post-operatively. They are usually applied by means of cotton-wool or gauze dabbed or rubbed lightly over the surface. The nature of the deodorant being used would of course determine its compatibility with the usual antiseptics, but it is probable that incompatibility would be experienced with most of them.

### Inheritance of Little's Disease

**Q.**—*A patient has one child suffering from Little's disease. There was no birth injury, and the labour was normal. What are the chances of any future children being similarly affected?*

**A.**—Little's disease or congenital spastic diplegia is probably not a single clinical entity. Some cases may be due to birth injury, others to foetal malnutrition, prenatal infection, or to unknown environmental causes. A fairly large proportion of the cases are due to recessive genes. In complete ignorance of the cause, as in this particular case, the chances of recurrence of the abnormality in a subsequent pregnancy can be only roughly estimated at one in twenty. However, no accurate assessment can be given until careful inquiry has been made into the possible incidence of similar conditions in near relatives. Even if such inquiry leads to negative results but the parents are found to be cousins, the case is probably of recessive genetic origin, and the chance of recurrence is one in four. A search for incompatibility of Rh or of ABO antigens in mother and child might also yield some relevant information.

### Penicillin for Osteomyelitis

**Q.**—*A man of 27 had osteomyelitis of the left leg following an air-raid injury in 1943; this cleared up after nearly eight months in hospital. Since then he has had twenty-four axillary abscesses. Would penicillin injections be of any value in such a case?*

**A.**—If these abscesses are metastatic, a focus of osteomyelitis still existing in the left leg or elsewhere, penicillin treatment alone would be useless. It usually fails in any chronic infection depending on the continued existence of an old-standing focus, particularly if this is located in bone. Organisms situated in a chronic abscess cavity or in an area of necrosed bone cannot be eradicated completely by penicillin, if only because such an area is not adequately permeated by the drug.

### Uterine Haemorrhage after Synthetic Oestrogens

**Q.**—*A woman of 51 has an erythematous condition of her face. A specialist prescribed 1 mg. stilboestrol daily for two months, then one month's rest. She now has uterine bleeding, though her menopause was three years ago, and is worried about the possibility of pregnancy. Can I reassure her that stilboestrol does not cause ovulation after the menopause and that pregnancy cannot supervene?*

**A.**—The uterine haemorrhage which may follow oestrogen therapy is anovular in type and is not true menstruation. Stilboestrol, at any rate when continuously applied, does not cause ovulation; indeed it depresses ovarian activity. The chances of pregnancy are therefore extremely remote and certainly no greater than if the stilboestrol had not been given.

The reawakening of endometrial activity is, however, a disadvantage in itself. If the treatment is continued endometrial hyperplasia and profuse bleeding may result. Already the case is one of "post-menopausal bleeding," and though the cause is probably the stilboestrol there remains the possibility that the patient may have a growth in the uterus. If it has not already been done a pelvic examination should be made to exclude any obvious lesion in the vagina and cervix. The dose of stilboestrol should be reduced or, unless the skin condition is clearly benefiting from it, the treatment discontinued. If in spite of this the bleeding continues or recurs then the only safe line of action is to carry out diagnostic curettage.

### Blood Thiocyanate Estimations

**Q.**—*Please describe the biochemical technique for the estimation of blood thiocyanate levels in cases of hypertension under treatment with potassium thiocyanate.*

**A.**—Three solutions are needed for the estimation of thiocyanate in serum and plasma: (*a*) 10% trichloracetic acid. (*b*) Ferric nitrate reagent—dissolve 20 g. crystalline ferric nitrate in 500 ml. distilled water; add 25 ml. concentrated nitric acid. (*c*) Thiocyanate standard (stock solution)—dissolve about 1 g. potassium thiocyanate in 500 ml. distilled water; titrate 20 ml. of a standard silver nitrate solution (made by dissolving 2.9195 g. silver nitrate in 1,000 ml. water) acidified with 5 ml. concentrated nitric acid against the thiocyanate solution, using ferric ammonium sulphate as an indicator; add the water necessary to make 20 ml. thiocyanate equivalent to exactly 20 ml. silver nitrate solution; check.

To 5 ml. of solution (*a*) add 5 ml. plasma or serum, shake well and stand for fifteen minutes; filter—the filtrate must be perfectly clear; measure 5 ml. filtrate and to it add 1 ml. of ferric nitrate reagent (*b*). Make three dilutions of stock thiocyanate solution: 100 ml. in a litre of water; 70 ml. in a litre of water; and 40 ml. in a litre of water (equivalent to 1.0 mg., 0.70 mg., and 0.40 mg. in 5 ml.). To 2.5 ml. of these three standards in three test-tubes add 2.5 ml. of solution (*a*) and 1 ml. of solution (*b*). Read the unknown against the standard in a colorimeter, using the standard which it most nearly matches.

It should perhaps be pointed out that since the appearance of Barker's work (*J. Amer. Med. Ass.*, 1936, **106**, 762 and 1941, **117**, 1591) the original theory that thiocyanate is deficient in hypertensive blood has been disputed. Later determinations have shown a normal content, and clinical experience of the thiocyanate treatment in this country has not fulfilled the hopes held out for it originally by American workers.

## INCOME TAX

### Car Transactions

R. M. bought an "M" car in 1940 for £180; he sold it in March, 1946, buying an "R" car for £710. No depreciation allowance has been claimed.

*** We suggest that he claims depreciation on the "M" car for the six years 1941–2 to 1946–7 inclusive; the claim should be made under Section 45 of the Finance Act, 1927, on the ground that overcharges have resulted from "errors or omissions in the returns." The amounts of depreciation apparently claimable are: 1941–2, £43; 1942–3, £35; 1943–4, £28; 1944–5, £21; 1945–6, £18, and 1946–7, £14. No depreciation in respect of the "R" car is due for 1946–7, but, assuming that the accounts of the practice are made up to Dec. 31 each year, allowance will be due for 1947–8 as follows:

| | | |
|---|---|---|
| Initial Allowance | 20% of £710 | £142 |
| Depreciation Allowance | 25% of £710 | £178 |
| Total | | £320 |

### Post-demobilization Appointment

"Resident" holds a Class 3 post-demobilization appointment. His salary is £550, which is paid by the hospital but made good by the Exchequer. Is the salary liable to income tax? If so, can the cost of journals and textbooks be claimed as a deduction, seeing that they are necessary for preparation for the higher degree which "Resident" is expected to take?

*** It is understood that payments of this nature are not "grants" in the true sense of the word, but are regarded as made by the hospital in respect of services rendered. On that basis they are liable to income tax. Similarly any sum paid for maintenance is subject to tax in the same way as the E.M.S. living-out allowance. The position as regards the cost of technical books, etc., is not free from doubt. To be allowable such expenses must be incurred "wholly, exclusively, and necessarily in the performance of the duties of the office." If "Resident" establishes the fact that one of the duties required of him is to prepare for the higher degree, the expense should be allowed as a deduction from the salary. The point may well be worth taking to appeal before the District Commissioners of Taxes if the local inspector of taxes is not willing to concede it.

### Research Grant

W. T. is in receipt of a research grant to provide for expenses and, to some degree, maintenance. The local tax office regards the grant as assessable to tax.

*** The question is governed by Sec. 28 of the Finance Act, 1920. The grant is exempt from tax if W. T. is receiving full-time instruction at a university, college, or other educational establishment. If—as appears probable—W. T. cannot claim to comply with this condition he will be liable to assessment in respect of the grant but should claim to deduct a reasonable amount for the expenses necessarily incurred in the research, the carrying out of which he is required to do under the terms of the grant. He is advised to call (preferably by appointment) at the tax office to explain what expenses he claims, and to raise the question of the tax deductions being made under P.A.Y.E. at present—they are apparently excessive and perhaps made because W. T. has not lodged a statement of income, etc.

# LETTERS, NOTES, ETC.

### Nomenclature of the Rh Blood Types

Dr. BRYCE R. NISBET (Hon. Sec., Ayrshire Division, B.M.A.) writes: Let me assure Lieut.-Col. G. E. W. Wolstenholme (Nov. 16, p. 753) that the lecture as delivered to the Ayrshire Division by Prof. Cappell was considerably simplified and illustrated by slides and drawings. We were thus able to see and listen and, as evidence that it was much appreciated, as many as eight of the forty-four members who were present took part in the discussion. We, north of the Cheviots, being such large consumers of porridge, like a little "meat" at our gatherings. It is about the only time we can have a surfeit. Whether we shall be able to stand it in the future is a matter of conjecture since oatmeal has been put on points.

### Definition of Health

Dr. D. F. TORRENS (Market Rasen) writes: Dr. W. F. Felton (Oct. 19, p. 591) raises the fundamental question. He says "surely complete physical, mental, and social well-being is a god-like state . . ." but he goes on to say that "we can hardly hope to attain [it], let alone claim [it] as our right." He prefers "a balanced state of physical, mental, and social well-being." Neither of these definitions is yet actual in the human race. Each is a statement of an objective to be worked for. There is a vast difference between them. The first is a statement of a belief in a god and that man's goal is to become like God, as Dr. Felton says. The second does not go nearly so far, though it might be pushed a good way in the same direction; it asks only for a balance, and that balance might be established at a very low standard. Also it is man who who will set the standard. It is because, in all our social legislation, the ideal expressed and implied is a super-man that the results are disappointing. The best man is not good enough, for though he is immortal he is transitory. Other men with other motives and methods take his place. This is seen in the proposed changes in medicine. Instead of a Ministry of Healing we are to have a huge business organization controlled by scientific analysis and economic theory. But there is nothing to control the controllers. Man is so puffed up (if not yet blown up) by his success (?) in splitting the atom that he has quite lost sight of the Almighty Power which *made* every atom. Such a mentality will never do good work. No one can who does not know his material. If medicine does not nail its colours to the mast, if it wavers in its loyalty to Christianity, it *must* become the tool of "scientific research" and the slave of "economic theory."

### Ichthyol

Dr. J. AITKEN MCEWEN (Barnsley) writes: In his letter (Nov. 23, p. 804) Surg. Lieut. G. B. Hopkins comments on the geological origin of ichthyol as being "the schist . . . regarded by geologists as having originated by fossilization of seabirds' excreta." My recollection (quoting, I believe, Poullsson's *Pharmacology*) is that ichthyol is derived from destructive distillation of a shale, found in the Dolomites, containing the teeth of fossilized fish. I always understood that this fact was responsible for the name of the product (*ἰχθύς* =a fish). While I lay no pretensions to any qualification in geology, I beg leave to doubt the statement that any schist could be the result of fossilization. I stand, however, prepared to be corrected in both statements.

### Effects of Penicillin Lozenges

Dr. A. J. COLBY TINGEY (Epsom) writes: Dr. I. G. Cameron (Oct. 26, p. 638) considers it would be of interest if doctors would write of their experiences with these lozenges. It appears possible that in some cases penicillin lozenges may actually lower the patient's resistance to bacterial infection. For example, in June last I was consulted by a patient aged 31 who had a mild form of tonsillitis with a temperature of 99° F. (37.2° C.), and at his request I gave him a prescription for penicillin lozenges. Three days later I received an urgent message from his wife, and found him in bed at home with a temperature of 104° F. (40° C.), and the usual symptoms of acute toxaemia. He was very ill for the next few days, but made a good recovery with sulphonamide treatment. I submit that acute tonsillitis is a general infection, and that to treat the complaint with penicillin lozenges is little better than a placebo. The attitude of the general public to penicillin may best be described by the Latin tag—"*Omne ignotum pro magnifico.*"

### Foreign Body in the Duodenum

Mr. D. LIVINGSTONE POW (Wrexham) writes: It is recognized that long objects—e.g., nails—are apt to become arrested in the second or third parts of the duodenum. The following case is of some interest. A female child aged 1 year and 11 months was admitted to the Wrexham and East Denbighshire War Memorial Hospital on Sept. 24, 1946, with a history of having swallowed the buckle of a pram-belt on Aug. 19. The child had been taken immediately to the Out-patient Department; but, although *x*-ray examination had demonstrated the foreign body and also the fact that it was remaining in the same place, no step was taken for a time, possibly because the radiologist was inclined to the opinion that the object was not in the stomach or duodenum. (A barium examination of the child was not easy because of struggling.) The child appeared perfectly well throughout the period between ingestion and operation. The latter was performed on Sept. 25. It was difficult, as usual, to locate the buckle, but it was finally detected in the second portion of the duodenum. Attempts to manipulate it downwards failed and for a time it could not be persuaded to move upwards. However, eventually it was felt to slip towards the pylorus, and while it was held there an incision was made in the anterior wall of the stomach near the antral area. A finger introduced into the interior of the stomach could feel the buckle presenting at the pyloric ring, but it was only with considerable difficulty that the object was finally persuaded sufficiently far through the pylorus to enable my house-surgeon—Dr. A. W. Fowler, who was assisting—to grip it with pressure forceps. The cause of the difficulty now became manifest. In the middle of one of the long sides of the rectangular buckle was an interval rather less than one-eighth of an inch (0.32 cm.) in length and in that a fold of duodenal mucosa had been caught. It was disentangled only with some effort, and thereafter the opening in the stomach was closed and the operation terminated. Convalescence was uneventful. The buckle measured one and a quarter inches by five-eighths of an inch (3.18 cm. by 1.60 cm.).

### Milk Priority

Dr. ESTHER CARLING writes: A striking instance of wasteful allotment of milk came to my notice recently. At a small holiday guest-house for ex-sanatorium patients (now workers) two pints of milk daily were being delivered for every guest. The housekeeper spoke of her difficulty in "getting rid of it." Such an occurrence suggests that the almost routine issue of two pints daily, sometimes over years, could surely be lessened in these times of stress.

Dr. W. J. LORD (Bath) writes: May I stress one point in the letters of Drs. H. E. Collier and G. B. Page (Nov. 16, p. 751), namely, milk priority for old people? Not only, in most cases, are their digestive functions inefficient, but they have the added burden of housework and shopping to a much larger extent than before the war. These hardships, again, are often aggravated by arterio-sclerosis and high blood pressure.

### Pronunciation of Medical Words

Dr. R. L. WYNNE (Wallasey) writes: The problems of pronunciation which have been given publicity in your columns arise from the difficulties of assimilation of foreign and dead stems into the living structure of a vigorous language, and in them usage might be expected to be variable and sometimes illogical. May I draw attention to another and more serious variety of mispronunciation?—the commonly used versions of foreign proper names, mostly by surgeons. This, curiously, seems related only to their profession. An orthopaedic surgeon who correctly recounts that he has admired the singing of Gigli the tenor, will later be heard calling for a "giggly" saw. The German "umlaut" suffers horribly. In such a name as Böhler it is usually ignored, whereas in its old-fashioned form, as in "von Graefe," it commonly acquires a separate syllabification of its own, combined this time with a bland disregard for the final "e." Weil and Wassermann are lucky men who generally get a near equivalent of their names. Trendelenburg, however, gets his accent displaced from the first to the second syllable, presumably because the Anglo-Saxon tongue, though accustomed to an accent on the first syllable, gets nervous when the end of the word is too far off. Another sufferer is Braun, who on English lips brings to mind a popular meat dish rather than the familiar colour represented by his name. Before we embark on what must be purely academic discussion of the pronunciation of words which in their origin are all neologisms, would it not be wise to set our house in order regarding words of whose pronunciation there is no doubt, once due attention is given to them?

Dr. A. R. NELIGAN (Droitwich) writes: Your correspondent Dr R. O'Rahilly (Nov. 9, p. 711) and other readers may be interested to know that, at a meeting of the International Society of Hydrology held at Buxton last month, an American doctor who read a paper pronounced the "e" of the word "syndrome" throughout.

Dr. MARGARET VIVIAN (Bournemouth) writes: Three of my colleagues have answered my question regarding the pronunciation of the word schizophrenia: two by letter, and one in your current issue. Each one gives a different version: (1) Shy-so; (2) Skitso; and (3) Skyzo. So it appears that we are, as it were, where we were.

### Corrigendum

In the leading article on "The Control of Air-borne Infection" (*Journal*, Nov. 30, p. 820) the word "mass" at the end of the twelfth line from the end should read "mess."